

# Freeform Search

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EPO Abstracts Database  
Derwent World Patents Index  
IBM Technical Disclosure Bulletins

Term:

L42 and (titanium)

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## Search History

DATE: Thursday, March 27, 2003 [Printable Copy](#) [Create Case](#)

Set Name Query  
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DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ

<u>L43</u>	L42 and (titanium)	0	<u>L43</u>
<u>L42</u>	L41 and (complex)	0	<u>L42</u>
<u>L41</u>	L40 and (pixel or voxel or locat\$8)	2	<u>L41</u>
<u>L40</u>	L39 and (phase)	2	<u>L40</u>
<u>L39</u>	L38 and (magnitude)	3	<u>L39</u>
<u>L38</u>	L36 and (prostate)	3	<u>L38</u>
<u>L37</u>	L36 and (prosate)	0	<u>L37</u>
<u>L36</u>	L35 and (((display\$4 or show\$4 or represent\$9) with implant\$4)	9	<u>L36</u>
<u>L35</u>	L34 and (graph\$9 with implant\$4)	9	<u>L35</u>
<u>L34</u>	L1 and (((brachytherapy or brachy-therapy ) with seed) or (seed with implant\$))	163	<u>L34</u>

<u>L33</u>	L32 and (((brachytherapy or brachy-therapy ) with seed) or (seed with implant\$))	1	<u>L33</u>
<u>L32</u>	l26 not l27	1	<u>L32</u>
<u>L31</u>	L28 not l30	8	<u>L31</u>
<u>L30</u>	L28 and (k-space or kspace or "k space" or raw)	2	<u>L30</u>
<u>L29</u>	L28 and (fourier or ft or fft or dft)	0	<u>L29</u>
<u>L28</u>	L27 and (complex)	10	<u>L28</u>
<u>L27</u>	L26 and (difference or subtract\$6)	10	<u>L27</u>
<u>L26</u>	L25 and (image\$2 or imaging)	11	<u>L26</u>
<u>L25</u>	L24 and (magnitude)	11	<u>L25</u>
<u>L24</u>	L23 and (phase)	115	<u>L24</u>
<u>L23</u>	L22 and (brachytherapy or brachy-therapy or seed)	133	<u>L23</u>
<u>L22</u>	L21 and (titanium)	273	<u>L22</u>
<u>L21</u>	L20 and (prostate)	642	<u>L21</u>
<u>L20</u>	L1 and ((implant\$4 or interventional or catheter or biopsy or needle or guidewire or guide-wire) with (device or apparatus or instrument))	4297	<u>L20</u>
<u>L19</u>	L18 and (prostate)	0	<u>L19</u>
<u>L18</u>	L17 and (implant\$4)	6	<u>L18</u>
<u>L17</u>	5730129	20	<u>L17</u>
<u>L16</u>	L4 and (prostate or brachytherapy or seed)	2	<u>L16</u>
<u>L15</u>	L13 and (brachy-therapy with seed)	0	<u>L15</u>
<u>L14</u>	L13 and (brachytherapy with seed)	0	<u>L14</u>
<u>L13</u>	L10 and (tissue or prostate or brachytherapy or seed)	10	<u>L13</u>
<u>L12</u>	L11 and (tissue or prostate or brachytherapy or seed)	1	<u>L12</u>
<u>L11</u>	L10 and (implant\$6 or imbed\$4 or embed\$4)	1	<u>L11</u>
<u>L10</u>	L9 and (group or set or data or plurality or first or second or third or primary or secondary or tertiary or supplemental or additional)	11	<u>L10</u>
<u>L9</u>	L8 and (phase with (image\$2 or imaging))	11	<u>L9</u>
<u>L8</u>	L7 and (spin-echo\$2 or "spin echo\$2" or spinecho\$2 or gre or (gradient with echo\$4) or fieldecho\$2 or field-echo\$2 or "field echo\$2" or Hahn)	11	<u>L8</u>
<u>L7</u>	L6 and (fourier or ft or fft or dft)	11	<u>L7</u>
<u>L6</u>	L5 and (k-space or kspace or "k space" or raw)	11	<u>L6</u>
<u>L5</u>	L4 and (complex)	17	<u>L5</u>
<u>L4</u>	L3 and (phase with difference with (image\$2 or imaging) with magnitude)	35	<u>L4</u>
<u>L3</u>	L2 and (phase with difference with (image\$2 or imaging))	125	<u>L3</u>
<u>L2</u>	L1 and (magnitude with (image\$2 or imaging))	1203	<u>L2</u>
<u>L1</u>	((magnetic adj resonance) or MRI or NMR)	143548	<u>L1</u>

END OF SEARCH HISTORY

## Freeform Search

Database:

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JPO Abstracts Database  
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Derwent World Patents Index  
IBM Technical Disclosure Bulletins

Term:

L16 and (phase or difference or complex or  
subtract\$4)

Display:  Documents in Display Format:  Starting with Number Generate: ☐ Hit List ☒ Hit Count ☐ Side by Side ☐ Image

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## Search History

DATE: Thursday, March 27, 2003 [Printable Copy](#) [Create Case](#)

**Set Name Query**  
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result set

*DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ*

<u>L17</u>	L16 and (phase or difference or complex or subtract\$4)	7	<u>L17</u>
<u>L16</u>	L15 and (seed)	7	<u>L16</u>
<u>L15</u>	L14 and (brachytherapy)	7	<u>L15</u>
<u>L14</u>	L10 and (titanium)	24	<u>L14</u>
<u>L13</u>	L12 and (titanium)	0	<u>L13</u>
<u>L12</u>	L11 and (magnitude)	4	<u>L12</u>
<u>L11</u>	L10 and (phase with difference)	7	<u>L11</u>
<u>L10</u>	L9 and (prostate)	145	<u>L10</u>
<u>L9</u>	L7 and (((position\$7 or locat\$7) with device or apparatus or instrument or catheter or guide-wire or guidewire or "guide wire" or needle) with "within" with (subject or object or patient))	1748	<u>L9</u>
<u>L8</u>	L7 and (((position\$7 or locat\$7) with device or apparatus or instrument or catheter or guide-wire or guidewire or "guide wire" or needle) with "within" with (subject or object or patient))	1748	<u>L8</u>
<u>L7</u>	((magnetic adj resonance or MRI or NMR))	143548	<u>L7</u>
<u>L6</u>	L3 and (prostate)	1	<u>L6</u>
<u>L5</u>	L3 and (((locat\$6 or position\$6) with implant\$4) with (phase with difference))	0	<u>L5</u>
<u>L4</u>	L3 and (((locat\$6 or position\$6) with implant\$4) with (phase with difference))	0	<u>L4</u>
<u>L3</u>	L2 and (phase with difference)	11	<u>L3</u>
<u>L2</u>	L1 and ((locat\$6 or position\$6) with implant\$4)	825	<u>L2</u>
<u>L1</u>	((magnetic adj resonance) or MRI or NMR)	143548	<u>L1</u>

END OF SEARCH HISTORY

## End of Result Set



Generate Collection

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L3: Entry 4 of 4

File: USPT

Jul 13, 1993

DOCUMENT-IDENTIFIER: US 5226418 A

TITLE: Phase correction of complex - difference processed magnetic resonance angiograms

US PATENT NO. (1):

5226418

Brief Summary Text (4):

When a substance such as human tissue is subjected to a uniform magnetic field (polarizing field  $B_{sub.0}$ ), the individual magnetic moments of the spins in the tissue attempt to align with this polarizing field, but precess about it in random order at their characteristic Larmor frequency. A net magnetic moment  $M_{sub.z}$  is produced in the direction of the polarizing field, but the randomly oriented magnetic components in the perpendicular, or transverse, plane (x-y plane) cancel one another. If, however, the substance, or tissue, is subjected to a magnetic field (excitation field  $B_{sub.1}$ ) which is in the x-y plane and which is near the Larmor frequency, the net aligned moment,  $M_{sub.z}$ , may be rotated, or "tipped", into the x-y plane to produce a net transverse magnetic moment  $M_{sub.t}$ , which is rotating, or spinning, in the x-y plane at the Larmor frequency. The degree to which the net magnetic moment  $M_{sub.z}$  is tipped (flip angle), and hence the magnitude of the net transverse magnetic moment  $M_{sub.t}$  depends primarily on the length of time and the magnitude of the applied excitation field  $B_{sub.1}$ .

Brief Summary Text (5):

The practical value of this phenomenon resides in the signal which is emitted by the excited spins after the excitation signal  $B_{sub.1}$  is terminated. In simple systems the excited spin induces an oscillating sine wave signal in a receiving coil. The frequency of this signal is the Larmor frequency, and its initial amplitude,  $A_{sub.0}$ , is determined by the magnitude of the transverse magnetic moment  $M_{sub.t}$  and the flip angle. The amplitude,  $A$ , of the emission signal decays in an exponential fashion with time,  $t$ :

Brief Summary Text (8):

The NMR measurements of particular relevance to the present invention are called "pulsed NMR measurements". Such NMR measurements are divided into a period of RF excitation and a period of signal emission. Such measurements are performed in a cyclic manner in which the NMR measurement is repeated many times to accumulate different data during each cycle or to make the same measurement at different locations in the subject. A wide variety of preparative excitation techniques are known which involve the application of one or more RF excitation pulses ( $B_{sub.1}$ ) of varying magnitude, duration, and direction. Such excitation pulses may have a narrow frequency spectrum (selective excitation pulse), or they may have a broad frequency spectrum (nonselective excitation pulse) which produces transverse magnetization  $M_{sub.t}$  over a range of resonant frequencies. The prior art is replete with excitation techniques that are designed to take advantage of particular NMR phenomena and which overcome particular problems in the NMR measurement process.

Brief Summary Text (11):

The present invention will be described in detail with reference to a variant of the well known Fourier transform (FT) imaging technique, which is frequently referred to as "spin-warp". The spin-warp technique is discussed in an article entitled "Spin Warp NMR Imaging and Applications to Human Whole-Body Imaging" by W. A. Edelstein et al., Physics in Medicine and Biology, Vol. 25, pp. 751-756 (1980). It employs a variable amplitude phase encoding magnetic field gradient pulse prior to the

acquisition of NMR spin-echo signals to phase encode spatial information in the direction of this gradient. In a two-dimensional implementation (2DFT), for example, spatial information is encoded in one direction by applying a phase encoding gradient (G.sub.y) along that direction, and then a spin-echo signal is acquired in the presence of a readout magnetic field gradient (G.sub.x) in a direction orthogonal to the phase encoding direction. The readout gradient present during the spin-echo acquisition encodes spatial information in the orthogonal direction. In a typical 2DFT pulse sequence, the magnitude of the phase encoding gradient pulse G.sub.y is incremented (.DELTA.G.sub.y) in the sequence of views that are acquired during the scan to produce a set of NMR data from which an entire image can be reconstructed.

Detailed Description Text (7):

Referring particularly to FIGS. 1 and 2, the transceiver 122 includes components which produce the RF excitation field B.sub.1 through power amplifier 123 at a coil 138A and components which receive the resulting NMR signal induced in a coil 138B. The base, or carrier, frequency of the RF excitation field is produced under control of a frequency synthesizer 200 which receives a set of digital signals through the communications link 103 from the main computer 101. These digital signals indicate the frequency and phase of the RF carrier signal which is produced at an output 201. The commanded RF Carrier is applied to a modulator 202 where it is modulated in response to a signal R(t) received through bus 103 from the PCM 120. The signal R(t) defines the envelope, and therefore the bandwidth, of the RF excitation pulse to be produced. It is produced in the PCM 120 by sequentially reading out a series of stored digital values as the RF excitation pulse is produced that represent the desired envelope. These stored digital values may, in turn, be changed by the computer 100 to enable any desired RF pulse envelope to be produced. The magnitude of the RF excitation pulse output through line 205 is attenuated by a transmit attenuator circuit 206 which receives a digital signal, TA, from the main computer 101 through communications link 103. The attenuated RF excitation pulses are applied to the power amplifier 123 that drives the RF transmitter coil 138A. For a more detailed description of this portion of the transceiver 122, reference is made to U.S. Pat. No. 4,952,877 which is incorporated herein by reference.

Detailed Description Text (20):

The processing of the k-space NMR data sets Z.sub.1 and Z.sub.2 to produce an angiogram is illustrated in FIG. 4. All of the processing is carried out in the main computer 101 under the direction of instructions in a stored program. The two k-space NMR data sets Z.sub.1 and Z.sub.2 are stored as 256 by 256 arrays of complex numbers indicated by blocks 320 and 321. The first step in the process is to perform a two-dimensional, complex Fourier transformation on each of these data sets 320 and 321 to transform the images they represent from k-space to the image domain. This is the same transformation used to produce conventional NMR images and the results are two 256 by 256 element arrays 322 and 323 of complex numbers (M.sub.1) and (M.sub.2). The magnitudes of the complex numbers M.sub.1 (x,y) and M.sub.2 (x,y) indicate the spin density at corresponding image pixel locations (x,y) and the phase of each complex number M.sub.1 (x,y) and M.sub.2 (x,y) is determined by both the velocity of the spins along the direction of the motion encoding magnetic field gradient G.sub.M and by any system phase errors. Any difference in these system phase errors in the two data sets produce image artifacts when a conventional complex-difference angiogram is produced using the image domain NMR data sets M.sub.1 and M.sub.2, and it is these phase errors which are substantially reduced by employing the teachings of the present invention.

Detailed Description Text (23):

Where x and y are position in the two imaging coordinates. While the method described herein is general enough to be compatible with nearly any phase correction method, in the preferred embodiment .phi..sub.1, .alpha. and .beta. are calculated using a least squares fit. It has been found that weighting the least square fit by the square of the average magnitude (A=(.vertline.M.sub.1 .vertline.+ .vertline.M.sub.2 .vertline.)/2) provides adequate suppression of regions of low signal. Thus, the least squares fit for .phi..sub.0, .alpha. and .beta. is: ##EQU2## The summations in the above equations are over all pixel values in the image array. The corrected phase .phi..sub.cor is thus calculated for each position x, y in the array 326 using Eq. 1, where .phi..sub.0, .alpha., and .beta. were calculated using the average magnitude values (A) and the phase difference values .phi. from the array 325. One important advantage of performing the phase correction on the phase image is that the correction can easily be extended to orders higher than linear.

Detailed Description Text (24):

A complex difference NMR data set is now calculated using the image domain NMR data sets 322 and 323, and the corrected phase difference array 326. This is accomplished by calculating each of 256 by 256 elements (D) in a complex difference data set 330 using the corresponding elements M.sub.1, M.sub.2 and .phi..sub.cor in the respective arrays 322, 323 and 326 and the following formula: ##EQU3## In other words, the magnitude data in the image domain NMR data sets 322 and 323 is used, but the phase difference information is not used. Instead, the corrected phase difference data .phi..sub.cor in the array 326 is employed so that artifacts produced by phase errors are eliminated from the resulting angiogram.



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☐ 1. Document ID: US 20010031037 A1

L10: Entry 1 of 11

File: PGPB

Oct 18, 2001

PGPUB-DOCUMENT-NUMBER: 20010031037

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010031037 A1

TITLE: Method for harmonic phase magnetic resonance imaging

PUBLICATION-DATE: October 18, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Prince, Jerry L.	Lutherville	MD	US	
Osman, Nael F.	Baltimore	MD	US	

US-CL-CURRENT: 378/137

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 2. Document ID: US 6408201 B1

L10: Entry 2 of 11

File: USPT

Jun 18, 2002

US-PAT-NO: 6408201

DOCUMENT-IDENTIFIER: US 6408201 B1

TITLE: Method and apparatus for efficient stenosis identification in peripheral arterial vasculature using MR imaging

DATE-ISSUED: June 18, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Foo; Thomas K. F.	Rockville	MD		
Ho; Vincent B.	North Bethesda	MD		

US-CL-CURRENT: 600/410; 324/300, 324/307, 382/128, 600/419, 600/420

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 3. Document ID: US 6332088 B1

L10: Entry 3 of 11

File: USPT

Dec 18, 2001

US-PAT-NO: 6332088  
DOCUMENT-IDENTIFIER: US 6332088 B1

TITLE: Method and apparatus for imaging instruments during interventional MRI using asymmetric spin echo sequences

DATE-ISSUED: December 18, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Zhang; Weigno	Foster City	CA		
Kaufman; Leon	San Francisco	CA		
Avram; Hector	Foster City	CA		

US-CL-CURRENT: 600/410; 324/307, 324/309, 324/310, 324/311, 324/312, 324/314, 324/318

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Draw Desc	Image									

☐ 4. Document ID: US 6317620 B1

L10: Entry 4 of 11

File: USPT

Nov 13, 2001

US-PAT-NO: 6317620  
DOCUMENT-IDENTIFIER: US 6317620 B1

TITLE: Method and apparatus for rapid assessment of stenosis severity

DATE-ISSUED: November 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ho; Vincent B.	North Bethesda	MD		
Foo; Thomas K. F.	Rockville	MD		

US-CL-CURRENT: 600/419; 324/306, 324/309, 600/420

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Draw Desc	Image									

☐ 5. Document ID: US 6292684 B1

L10: Entry 5 of 11

File: USPT

Sep 18, 2001

US-PAT-NO: 6292684  
DOCUMENT-IDENTIFIER: US 6292684 B1

TITLE: Respiratory displacement and velocity measurement using navigator MRI echo signals

DATE-ISSUED: September 18, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Du; Yiping	Towson	MD		
McVeigh; Elliot R.	Timonium	MD		

US-CL-CURRENT: 600/410; 324/309

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 6. Document ID: US 6275038 B1

L10: Entry 6 of 11

File: USPT

Aug 14, 2001

US-PAT-NO: 6275038

DOCUMENT-IDENTIFIER: US 6275038 B1

TITLE: Real time magnetic field mapping using MRI

DATE-ISSUED: August 14, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Harvey; Paul R.	Tel-Shalom, Karkoor		37074	IL

US-CL-CURRENT: 324/309; 324/307

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 7. Document ID: US 6150814 A

L10: Entry 7 of 11

File: USPT

Nov 21, 2000

US-PAT-NO: 6150814

DOCUMENT-IDENTIFIER: US 6150814 A

TITLE: Methods of achieving phase contrast in magnetic resonance imaging and a related apparatus

DATE-ISSUED: November 21, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Redpath; Thomas William Tennant	Aberdeen			GB
McKiddie; Fergus Iain	Laurencekirk			GB
Dymond; Rosemary Carmen	Cardiff			GB

US-CL-CURRENT: 324/307; 324/309

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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☐ 8. Document ID: US 6091243 A

L10: Entry 8 of 11

File: USPT

Jul 18, 2000

US-PAT-NO: 6091243

DOCUMENT-IDENTIFIER: US 6091243 A

TITLE: Water-fat imaging with direct phase encoding (DPE)

DATE-ISSUED: July 18, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Xiang; Qing-San	Vancouver			CA
An; Li	Vancouver			CA

US-CL-CURRENT: 324/307; 324/309

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMOC
Draw. Desc	Image									

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☐ 9. Document ID: US RE36679 E

L10: Entry 9 of 11

File: USPT

May 2, 2000

US-PAT-NO: RE36679

DOCUMENT-IDENTIFIER: US RE36679 E

TITLE: Method of cancelling ghosts from NMR images

DATE-ISSUED: May 2, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Zakhor; Avidesh	Encino	CA		
Rzedzian; Richard R.	Lexington	MA		

US-CL-CURRENT: 324/312; 324/307, 324/309

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMOC
Draw. Desc	Image									

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☐ 10. Document ID: US 5352979 A

L10: Entry 10 of 11

File: USPT

Oct 4, 1994

US-PAT-NO: 5352979

DOCUMENT-IDENTIFIER: US 5352979 A

TITLE: Magnetic resonance imaging with contrast enhanced phase angle reconstruction

DATE-ISSUED: October 4, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Conturo; Thomas E.	Baltimore	MD	21231	

US-CL-CURRENT: 324/307; 600/410, 600/413, 600/420

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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☐ 11. Document ID: US 5226418 A

L10: Entry 11 of 11

File: USPT

Jul 13, 1993

US-PAT-NO: 5226418

DOCUMENT-IDENTIFIER: US 5226418 A

TITLE: Phase correction of complex - difference processed magnetic resonance angiograms

DATE-ISSUED: July 13, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bernstein; Matthew A.	Waukesha	WI		
Pelc; Norbert J.	Los Altos	CA		

US-CL-CURRENT: 600/419; 324/306, 324/309

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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DATA.DWPI,TDBD,EPAB,JPAB,USPT,PGPB.	2444006
DATUM.DWPI,TDBD,EPAB,JPAB,USPT,PGPB.	22939
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☐ 1. Document ID: US 6091243 A

L12: Entry 1 of 1

File: USPT

Jul 18, 2000

US-PAT-NO: 6091243

DOCUMENT-IDENTIFIER: US 6091243 A

TITLE: Water-fat imaging with direct phase encoding (DPE)

DATE-ISSUED: July 18, 2000

**INVENTOR-INFORMATION:**

NAME	CITY	STATE	ZIP CODE	COUNTRY
Xiang; Qing-San	Vancouver			CA
An; Li	Vancouver			CA

US-CL-CURRENT: 324/307; 324/309

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
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PROSTATES.DWPI,TDBD,EPAB,JPAB,USPT,PGPB.	529
BRACHYTHERAPY.DWPI,TDBD,EPAB,JPAB,USPT,PGPB.	879
BRACHYTHERAPIES.DWPI,TDBD,EPAB,JPAB,USPT,PGPB.	2
BRACHYTHERAPYS	0
SEED.DWPI,TDBD,EPAB,JPAB,USPT,PGPB.	135889
SEEDS.DWPI,TDBD,EPAB,JPAB,USPT,PGPB.	64405
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L12: Entry 3 of 4

File: USPT

Aug 25, 1998

DOCUMENT-IDENTIFIER: US 5797849 A

TITLE: Method for carrying out a medical procedure using a three-dimensional tracking and imaging system

Abstract Text (1):

A method for carrying out a medical procedure using a 3-D tracking and imaging system (1600). A surgical instrument, such as a catheter, probe, sensor, needle or the like is inserted into a living being, and the position of the surgical instrument is tracked as it moves through a medium in a bodily structure. The location of the surgical instrument relative to its immediate surroundings is displayed to improve a physician's ability to precisely position the surgical instrument. The medical procedures including removal of an obstruction from the circulatory system, a biopsy, amniocentesis, brain surgery, measurement of cervical dilation, evaluation of knee stability, assessment of myocardial contractibility, eye surgery, prostate surgery and transmyocardial myocardial revascularization (TMR). In addition, the method of the present invention also finds use in connection with the generation of 2-D echo planes.

Detailed Description Text (7):

An 8-bit magnitude comparator (d5) is used to equate the manually set dip switch with address lines polled by the computer mother board. When a match is found, a signal is generated which gates demultiplexes d8 and d9, each of which is a 1-of-8 demultiplexes. The lower three address lines (A1-A3) are used as inputs to both of these Read and Write demultiplexes. To distinguish their functionality, the buffered IOR signal is sent to opposite polarity enables on each demultiplexer. Thus if IOR is in a high state, the system computer interface is in a Write mode. To avoid Reading and Writing from the I/O address ports, A4 is also used as an opposite polarity input to do and do. This has the effect of offsetting the Reads from the Writes by precisely 10 (hex) (i.e., 24). The result of this is two controllable ranges of eight data bits used for gating "reads" from the digital boards, and "writes" to the digital boards. A single PLD (d6) serves to handle the glue logic between the other components of the decoder circuitry.

Detailed Description Text (9):

The only remaining control line extending to the digital circuit card is the Address Enable (EN). This signal is used in conjunction with the I/O Read and I/O Write signals to gate the magnitude comparator (d5). By doing so, Direct Memory Access (IQMA) conflicts are avoided between the tracking system and other internal computer modules of the PC.

Detailed Description Text (23):

A second major function of the counter module or card is to provide an analog signal to output. Despite the fact that digital data acquisition is superior in many ways to conventional analog circuitry, many users are required to work with analog signals. The Digital-to-Analog (DAC) converter (s17) is thereby provided as an option on the standard tracking units of the preferred embodiment. The DAC of the present invention operates as follows. Successive 8-bit values are latched into one side of the one of four magnitude comparator (s15b, d, f & h). These values are selectable through the software to permit any combination of transmitter/receiver output signals to be transferred to the four analog outputs. The opposite side of each comparator (s15b, d, f & h), is directly connected to the constantly cycling transmitter and receiver bits. When the value applied to both sides of a comparator are equal, the output is passed to a 4-to-2 line encoder (s16), before being passed to a DAC (s17). Under this configuration, four distinct, 12-bit analog channels can be connected to an output port from the computer.

Detailed Description Text (51):

Imaging modality system 1624 acquires 2-D, 3-D or 4-D image data sets from an imaging source, such as fluoroscopy, an MRI (magnetic resonance imaging), CT (computerized tomography) or 2-D or 3-D ultrasound device, to provide a "template" through or against which the shape, position and movement of instrument 1670 being tracked can be displayed. The template typically takes the form of an image of the environment surrounding the instrument (e.g., a bodily structure). It should be noted that if multiple (3-D) volumes are acquired at different time intervals, a 4-D image is obtained (i.e., 3-D image changing over time).

Detailed Description Text (57):

The process begins with the PC that houses the digital circuit boards. The PC completes a data acquisition cycle and has many numbers in memory, each corresponding to a time that the ultrasound pulse took to travel the distance between all combinations of transducers within the measuring volume (module 1100). Within this volume, there exist a number of mobile transducers mounted on the instruments being tracked (see FIG. 9), as well as reference transducers located on the patient in strategic reference locations (see FIG. 15). The reference transducers may be mounted internal to the patient to provide an internal reference frame, or mounted external to provide an external reference frame. This propagation delay measure, or "signal", can be corrupted with noise, accordingly some signal processing may be needed to be performed to recover the likely values of the original signal (module 1102). This can be done by testing for the range of the signal, and by smoothing or predictive fitting to previous trajectories of the data signal.

Detailed Description Text (84):

The current method of tracking catheters involves frequent exposure of the patient to an x-ray source. Each successive x-ray provides information on the movement of the catheters within the patient. In addition, contrast agents are frequently injected into patients during catheter procedures. These injections can provide further information on the actual location of the catheter and help physicians to plan subsequent catheter movements.

Detailed Description Text (87):

1) The need for using harmful x-rays and contrast agents are virtually eliminated while determining the location of catheters within the patient;

Detailed Description Text (122):

The conventional method for guiding probes involves rigidly fastening the patient's head to a stereotactic frame by placing screws and pins into the patient's skull. The patient, with the frame attached, is then imaged using MRI or CAT, and a 3-D reconstruction of the patient's head is created. Pathologic tissue or lesions, such as tumors, are then precisely located relative to the frame. The patient is then taken to the operating room and the required instruments, such as electrodes or ablaters, are affixed to guides that allow the instruments to be moved along the specific paths into the patient's head. Once the surgical instrument is in place, the lesion can be corrected, destroyed or treated in some way. The foregoing approach is tedious, costly and subject to measurement error in translating the 3-D coordinates from the images to the actual position of the probes within the stereotactic frame.

Detailed Description Text (126):

As the probe is inserted into the head, its movement relative to the reference transducers can be tracked in real time 3-D. The probe will be inserted into the brain, toward the lesion which is visible on a 3-D data set that was previously acquired through CT or MRI. Accordingly, the path of the probe is followed on a computer screen toward the lesion, rather than actually looking at the brain. The lesion itself is located by the position using MRI or CT imaging. The reference transducers affixed to the patient's head can be imaged along with the patient, simplifying the registration process, and since they are affixed to the head, movements of the head relative to the operating table do not pose a problem with respect to tracking. Since the sound path is inside the patient's head, surgeons have complete freedom to move about the patient. As in the catheter guidance system (CGS) described above, the location of the probes is tracked with respect to a reference system. For the head and brain, the most appropriate reference system are 3-D MRI images.

Detailed Description Text (128):

The system for carrying out the foregoing procedure would preferably be comprised of the 3-D locating and imaging system described in detail above. Several transducers (PZT or PVDF) are mounted on the surgical probe to be inserted into the brain. Reference transducers are mounted either on the outside of the skull, or slid inside the head, between the brain and the skull. The reference transducers placed on the outside of the patient's head may be taped on or include adhesive backing tape. The reference transducers inserted into the brain will be anchored by sutures, hooks, or simply by friction alone. The patient may be imaged using MRI, CT, or any other multidimensional imaging modality, with the reference transducers in place. Accordingly, a volume reconstruction of the patient's head would be obtained. The reference transducer may be fitted with components that would enable them to be clearly seen on the 3-D image sets. A physician could then locate the lesion, or plan the surgical approach with respect to these referenced transducers. For example, the physician could draw a path in 3-D space that would be optimal to follow during the procedures. This path, as well as the intended location of the end point of the procedure, would be recorded by the computer system. The physician could also mark the location of the multiple transducers on the 3-D images, so that the computer system could register the physical location of the transducers to a location in the 3-D image space. It should be appreciated that depending on where the lesion is located in the brain, the surgical probe will be inserted from a different direction. Moreover, it is often necessary to go around critical areas so that minimal damage is done to the brain during insertion of the surgical probe.

Detailed Description Text (135):

The 3-D tracking and imaging system described above dramatically improves the precision for the foregoing procedures. As in the case of brain surgery, a 3-D image set of the cerebral vasculature is obtained and the progression through the vasculature may be monitored by projecting the position of the catheter within the 3-D scene of the vasculature. This may be done by mounting appropriate PZT or PVDF transducers on the catheters and tracking them as described above. The 3-D scene of the cerebral vasculature may be obtained through a CT scan with contrast agent injected into the patient, or with MRI tuned to show moving blood. Similar to the brain surgery procedure described above, transducers are arranged on the catheter and reference transducers are arranged on the patient's head. It should be noted that the placement of the external reference transducers is dictated by the location of "ultrasound" windows that enable signals to be sent into the skull. Accordingly, the preferred position for the reference transducers are the base of the head near the back, the eye sockets, or under the chin.

Detailed Description Text (147):

xi) PROSTATE SURGERY

Detailed Description Text (148):

Prostate surgery may be required when a prostate has become enlarged. This condition can cause such problems as incontinence and impotence. In many cases, the enlarged prostate is caused by a tumor. The tumor will need to be destroyed or removed, otherwise it may spread and kill the patient.

Detailed Description Text (149):

As in the case of eye surgery, 3-D ultrasound is useful in the diagnosis of prostate tumors. 3-D ultrasound may be used to visualize the size and shape of the prostate and may also be used to aid in stereotactic surgery of the prostate. However, it should be noted that 3-D ultrasound typically gives poor quality images and does not provide real time position feedback. Accordingly, there is a need to track the position of the surgical probes in real time using some other modality. The approach used in connection with the prostate and other internal organs would be essentially the same as the approach used in connection with the eye. In this respect, the organ of interest would be imaged using 3-D ultrasound, and the probes visualized with the 3-D tracking and imaging system of the present invention, as the probes are manipulated through the organ. The region to be treated is initially determined using an x-ray or ultrasound.

Detailed Description Text (160):

Transducer housing 1704 holds three or more position transducers 1706 that form a plane perpendicular to the imaging beam. Thus, position transducers 1706 reside between the imaging head 1700 and the skin that imaging head 1700 contacts. It should be appreciated that while four position transducers 1706 are shown in FIGS. 17A and 17B, only three position transducers 1706 are need to measure all angles. Reference transducers (not shown) are mounted to the patient's skin (e.g., back

and abdomen). As the imaging head 1700 is tilted and angulated while pressed against the abdomen, the coordinates of position transducers 1706 define a plane that is perpendicular to the ultrasound imaging beam. It should be noted that transducer housing 1704 makes contact with the abdomen. Once the position and orientation of the imaging plane is known in 3-D space relative to the coordinate system of the patient, the typical pie-shaped sector scan produced by the ultrasound imaging head can be inserted into the 3-D scene of the patient. The 3-D scene will therefore contain a perspective rendering of the patient frame of reference, the location and direction of the surgical instrument (e.g., amniocentesis needle), and the pie-shaped, ultrasound sector image, properly oriented within this scene, as shown in FIG. 18.

Detailed Description Text (163):

The foregoing description provides specific embodiments of the present invention. It should be appreciated that these embodiments are described for purposes of illustration only, and that numerous alterations and modifications may be practiced by those skilled in the art without departing from the spirit and scope of the invention. For instance, it should be appreciated that the transducers may use the time of flight, or phase differences as a means of determining position. Moreover, the transducers may take the form of ultrasonic transducers or electromagnetic transducers. It is intended that all such modifications and alterations be included insofar as they come within the scope of the invention as claimed or the equivalents thereof.

CLAIMS:

14. The method as defined in claim 2, wherein said medical procedure is prostate surgery, and said instrument is a medical probe moved through the prostate.

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☐ 1. Document ID: US 20010031037 A1

L13: Entry 1 of 10

File: PGPB

Oct 18, 2001

PGPUB-DOCUMENT-NUMBER: 20010031037

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010031037 A1

TITLE: Method for harmonic phase magnetic resonance imaging

PUBLICATION-DATE: October 18, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Prince, Jerry L.	Lutherville	MD	US	
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US-CL-CURRENT: 378/137

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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☐ 2. Document ID: US 6408201 B1

L13: Entry 2 of 10

File: USPT

Jun 18, 2002

US-PAT-NO: 6408201

DOCUMENT-IDENTIFIER: US 6408201 B1

TITLE: Method and apparatus for efficient stenosis identification in peripheral arterial vasculature using MR imaging

DATE-ISSUED: June 18, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Foo; Thomas K. F.	Rockville	MD		
Ho; Vincent B.	North Bethesda	MD		

US-CL-CURRENT: 600/410; 324/300, 324/307, 382/128, 600/419, 600/420

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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☐ 3. Document ID: US 6332088 B1

L13: Entry 3 of 10

File: USPT

Dec 18, 2001

US-PAT-NO: 6332088  
DOCUMENT-IDENTIFIER: US 6332088 B1

TITLE: Method and apparatus for imaging instruments during interventional MRI using asymmetric spin echo sequences

DATE-ISSUED: December 18, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Zhang; Weigno	Foster City	CA		
Kaufman; Leon	San Francisco	CA		
Avram; Hector	Foster City	CA		

US-CL-CURRENT: 600/410; 324/307, 324/309, 324/310, 324/311, 324/312, 324/314, 324/318

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Drawn Desc	Image									

☐ 4. Document ID: US 6317620 B1

L13: Entry 4 of 10

File: USPT

Nov 13, 2001

US-PAT-NO: 6317620  
DOCUMENT-IDENTIFIER: US 6317620 B1

TITLE: Method and apparatus for rapid assessment of stenosis severity

DATE-ISSUED: November 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ho; Vincent B.	North Bethesda	MD		
Foo; Thomas K. F.	Rockville	MD		

US-CL-CURRENT: 600/419; 324/306, 324/309, 600/420

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
Drawn Desc	Image									

☐ 5. Document ID: US 6292684 B1

L13: Entry 5 of 10

File: USPT

Sep 18, 2001

US-PAT-NO: 6292684  
DOCUMENT-IDENTIFIER: US 6292684 B1

TITLE: Respiratory displacement and velocity measurement using navigator MRI echo signals

DATE-ISSUED: September 18, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Du; Yiping	Towson	MD		
McVeigh; Elliot R.	Timonium	MD		

US-CL-CURRENT: 600/410; 324/309

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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☐ 6. Document ID: US 6275038 B1

L13: Entry 6 of 10

File: USPT

Aug 14, 2001

US-PAT-NO: 6275038

DOCUMENT-IDENTIFIER: US 6275038 B1

TITLE: Real time magnetic field mapping using MRI

DATE-ISSUED: August 14, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Harvey; Paul R.	Tel-Shalom, Karkoor		37074	IL

US-CL-CURRENT: 324/309; 324/307

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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☐ 7. Document ID: US 6150814 A

L13: Entry 7 of 10

File: USPT

Nov 21, 2000

US-PAT-NO: 6150814

DOCUMENT-IDENTIFIER: US 6150814 A

TITLE: Methods of achieving phase contrast in magnetic resonance imaging and a related apparatus

DATE-ISSUED: November 21, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Redpath; Thomas William Tennant	Aberdeen			GB
McKiddie; Fergus Iain	Laurencekirk			GB
Dymond; Rosemary Carmen	Cardiff			GB

US-CL-CURRENT: 324/307; 324/309

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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☐ 8. Document ID: US 6091243 A

L13: Entry 8 of 10

File: USPT

Jul 18, 2000

US-PAT-NO: 6091243

DOCUMENT-IDENTIFIER: US 6091243 A

TITLE: Water-fat imaging with direct phase encoding (DPE)

DATE-ISSUED: July 18, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Xiang; Qing-San	Vancouver			CA
An; Li	Vancouver			CA

US-CL-CURRENT: 324/307; 324/309

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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☐ 9. Document ID: US 5352979 A

L13: Entry 9 of 10

File: USPT

Oct 4, 1994

US-PAT-NO: 5352979

DOCUMENT-IDENTIFIER: US 5352979 A

TITLE: Magnetic resonance imaging with contrast enhanced phase angle reconstruction

DATE-ISSUED: October 4, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Conturo; Thomas E.	Baltimore	MD	21231	

US-CL-CURRENT: 324/307; 600/410, 600/413, 600/420

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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☐ 10. Document ID: US 5226418 A

L13: Entry 10 of 10

File: USPT

Jul 13, 1993

US-PAT-NO: 5226418

DOCUMENT-IDENTIFIER: US 5226418 A

TITLE: Phase correction of complex - difference processed magnetic resonance angiograms

DATE-ISSUED: July 13, 1993

INVENTOR-INFORMATION:



NAME	CITY	STATE	ZIP CODE	COUNTRY
Bernstein; Matthew A.	Waukesha	WI		
Pelc; Norbert J.	Los Altos	CA		

US-CL-CURRENT: 600/419; 324/306, 324/309

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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Term	Documents
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TISSUES.DWPI,TDBD,EPAB,JPAB,USPT,PGPB.	122687
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L13: Entry 9 of 10

File: USPT

Oct 4, 1994

DOCUMENT-IDENTIFIER: US 5352979 A

TITLE: Magnetic resonance imaging with contrast enhanced phase angle reconstructionAbstract Text (1):

The magnetic resonance image of a specimen is encoded by the phase angle response of the volume elements in a slice or volume illuminated by a pulsed radio frequency source, instead of encoded by the magnitude response. The specimen can be imaged before and during intrinsic perturbations such as caused by external stimuli or execution of cognitive or motor tasks. Preferably the specimen is perfused with a paramagnetic contrast agent such as Gadolinium or Dysprosium, slowly or by bolus injection, after recording one or more baseline images. The phase angle response of the specimen can then be recorded one or more times as perturbation subsists or as the bolus traverses the area of illumination. Fast Fourier transformation converts gradient spin echo response data to phase angles for a spatial distribution of volume elements in the illuminated slice. The baseline phase angle image is subtracted from the image taken after the bolus injection, providing a high contrast image showing the concentration of the contrast agent. The change .DELTA..phi. in phase angle between the images is proportional to the concentration of the contrast agent, enabling accurate measurements of localized blood volume and flow rate. The invention is particularly applicable to visualization of localized ischemia caused by cerebral vascular disease, such as stroke.

Brief Summary Text (3):

The invention relates to the field of magnetic resonance imaging for obtaining a graphic representation of biological samples and other materials, such as polymers, etc. (hereinafter, the "sample" or the "specimen"). In connection with graphic representation of tissue and the like, the invention provides a diagnostic tool for visualizing ischemia, infarction and other irregularities in cerebral and noncerebral tissues. However, the invention is useful for visualizing the microstructure of materials generally. More particularly, the invention employs phase angle reconstruction imaging techniques using paramagnetic contrast agents for improving the accuracy of the image data collected for each volume element in an image slice.

Brief Summary Text (5):

Magnetic resonance imaging is a non-invasive and non-destructive testing procedure whereby local variations in the electromagnetic properties of a specimen can be detected and displayed, for example, as variations in the luminance or color of pixels in an image. In general, magnetic resonance imaging involves applying bursts of radio frequency energy to a specimen positioned in a main magnetic field in order to produce responsive emission of electromagnetic radiation from hydrogen nuclei or other nuclei. The emitted signal is sampled over time after a predetermined time delay following an illuminating pulse, the time delay being chosen to highlight magnetically responsive atoms. The collected signal is digitized, producing a time domain representation of the specimen, typically through a plane or slice of predetermined thickness. By Fourier transform analysis the time domain representation is converted into a spatial representation of the slice, which is then displayed as an X-Y array of pixels. Whereas certain atoms contained in tissues are magnetically responsive at particular echo times and others are not, the resulting data can be used to distinguish between types of tissue, using the electromagnetic response of the tissue as the distinguishing parameter.

Brief Summary Text (6):

A plurality of slices can be recorded in this manner, for obtaining a three dimensional representation of the internal character of the specimen. The distinct

magnetic properties of the tissues are mapped to identify variations in anatomical structures. For example, the iron content in blood renders the blood more susceptible to magnetization than surrounding tissues, providing a means by which vascular structures can be distinguished. There are many particular methods by which data collected in this manner can be analyzed to produce useful information, with better detail than can be obtained from ultrasound imaging, without subjecting the specimen to ionizing radiation, and without undertaking surgery.

Brief Summary Text (7):

The Fourier transform involves converting the in-phase and out-of-phase signal amplitudes as a function of time to complex signal intensity as a function of frequency, from which the magnitude of the complex signal is derived. The magnitude data may be displayed without enhancement, but enhancement is valuable for presenting the information in variations of luminance, saturation and/or hue corresponding to structural variations thereby detected in heterogeneous tissue or the like. A specific technique for spin echo magnetic resonance imaging is disclosed, for example, in U.S. Pat. No. 4,766,381--Conturo et al. Once the raw data is available in the form of amplitude samples, various techniques can be employed for extracting useful data. However, there are certain limitations in the data due to the interaction of fields produced in neighboring tissues, motion in the blood vessels, etc.

Brief Summary Text (8):

In connection with certain conditions, a magnetic resonance image can be analyzed by skilled persons to visualize the location, size and character of tumors, hematomas, infarctions and the like, due to the spatially discontinuous response of such structures and/or the blood flow in the region to a pulsed radio frequency signal. For example, a localized area of anemic tissue may occur in connection with an infarction, and be identifiable as distinct from healthy surrounding tissue. The localized area or the perimeter of the area is characterized by a different magnetic susceptibility as a result of accumulation or scarcity of paramagnetic elements as compared to the healthy tissue. In the area of an injury, breakdown products of blood may accumulate, including deoxyhemoglobin, methemoglobin, free ferric iron, hemosiderin and the like.

Brief Summary Text (9):

Magnetic susceptibility data for imaging tissues including paramagnetic elements can be obtained by measuring the amplitude of transverse magnetization that remains after a change is induced by an incident radio frequency field. The net transverse decay rate differs for different areas of heterogeneous tissue, as a function of the local concentration and distribution of paramagnetic material.

Brief Summary Text (10):

It is possible to increase the contrast of a magnetic resonance image by infusing a paramagnetic material which has a different distribution in the structure of interest than the distribution in adjacent structures. Use of an exogenous agent to improve amplitude contrast is disclosed, for example, in "Perfusion Imaging with NMR Contrast Agents," Rosen et al, 14 Magnetic Resonance in Medicine 249-265 (1990).

Brief Summary Text (11):

Paramagnetic infusion can be effected by slow intravenous injection of an accumulating paramagnetic material, or by faster injection of a quantity of the paramagnetic material (i.e., a bolus), which travels through the blood stream. By recording a plurality of magnetic resonance images both before and during the perfusion of the tissues with blood carrying the paramagnetic contrast agent, it is possible to obtain a baseline image which can be subtracted from or divided into the signal magnitude data representing an image recorded during perfusion, thereby substantially enhancing the contrast and the detail of the particular structure of interest.

Brief Summary Text (12):

Subtraction of a baseline image from an image recorded during perfusion with an x-ray absorptive agent is known in connection with angiography. See, e.g., the references mentioned in "Projective Imaging of Pulsatile Flow with Magnetic Resonance," Wedeen et al, 230 Science 946-948 (1985). This article also discusses subtracting a baseline magnetic resonance complex image from a second image, the magnitude difference of which highlights moving elements (i.e., blood flow). The motion of the blood is detectable as magnitude signal changes which result from phase variation caused by the motion, producing a high contrast image of vascular

structures. However, the article does not discuss the possibility of relating contrast agents to magnetic resonance phase mapping, particularly in connection with phase angle reconstruction and baseline phase angle subtraction.

Brief Summary Text (13):

Magnetic susceptibility-weighted magnitude magnetic resonance images can be used in conjunction with bolus injection of paramagnetic contrast agents to assess the effects of cerebral perfusion. By rapidly acquiring such images (including at the time of passage of the bolus), functional aspects of cerebral blood flow can be identified. With a bolus injection, the paramagnetic agent is confined to the vascular space during passage through the brain, and later becomes diffused through the tissues in the remainder of the body.

Brief Summary Text (14):

Within the blood vessel, a bulk magnetic field shift is produced due to the paramagnetic susceptibility of the contrast agent. Field gradients occur around concentrations of the agent, e.g., around blood vessels. In a particular volume element (or "voxel") of brain parenchyma from which an image pixel is derived, there are complex field inhomogeneities that are not all due to corresponding inhomogeneities in the tissue structure or to inhomogeneities in the externally applied static field. The variations in field gradients produce signal dephasing that degrades the magnitude reconstructed signal of a magnetic resonance image. The signal loss depends on the statistical distribution of fields within the voxel (e.g., Gaussian vs. Lorentzian), and thus depends on factors such as the size, density and heterogeneity of capillaries as well as temporal concentration changes, multiexponential T<sub>2</sub> decay, diffusion and other factors.

Brief Summary Text (15):

The present invention is directed to phase reconstruction of an image rather than magnitude (amplitude) reconstruction, and thus relies on the variation in electromagnetic phase response of different tissues. Bulk magnetic susceptibility variations from tissue to tissue and variations due to hyperfine electron-nuclear coupling are enhanced by introduction of a paramagnetic contrast agent. The contrast agent causes resonance frequency shifts and field-frequency offsets which are detected as phase shifts using a phase angle reconstruction of the sampled data, preferably with subtraction of baseline data collected either before introduction of the contrast agent or after the contrast agent has diffused to the point that local inhomogeneities have dissipated.

Brief Summary Text (16):

The net phase is relatively insensitive to the intra-voxel field distribution, provided that the field distribution has a symmetric (e.g., statistical) profile, and thus can improve over results obtained in magnitude reconstruction, where many confounding factors contribute to signal dephasing. Paramagnetic-induced heterogeneities can be expected to induce different responses as to magnitude and phase, but the insensitivity of phase to at least some of these variations is such that phase reconstruction is believed to have better accuracy than magnitude reconstruction. Moreover, the phase images are better in a diagnostic setting, for example because the unaffected grey matter appears to have a more uniform brightness.

Brief Summary Text (17):

There are a limited number of examples where phase angle data has been collected for reconstruction of images representing variations in magnetic susceptibility. Such phase data has been used to image susceptibility variations which are endogenous to the brain, whereas the present invention provides a method by which phase angle reconstruction can be applied to exogenous paramagnetic enhancement, with favorable results as explained more fully hereinafter.

Brief Summary Text (19):

It is an object of the invention to improve the contrast and information content of a magnetic resonance imaging system by using susceptibility contrast enhancement via an exogenous paramagnetic contrast agent and baseline image subtraction.

Brief Summary Text (20):

It is another object of the invention to dynamically acquire phase angle images during bolus paramagnetic contrast injection in perfused cerebral or extracerebral tissues.

Brief Summary Text (21):

It is a further object to enable measurement of proportions of blood volume and tissue volume in a region of interest.

Brief Summary Text (22):

It is also an object of the invention to identify dependably certain cerebral and extracerebral conditions characterized by altered distribution of a paramagnetic contrast agent, including distinction between normal perfused tissues and abnormal tissues affected by stroke, ischemia, hematoma, infection, tumors and the like.

Brief Summary Text (23):

These and other objects are accomplished by a method and apparatus whereby a magnetic resonance image of a specimen is encoded by the phase angle response of the volume elements in a slice illuminated by a pulsed radio frequency source, instead of encoded by the magnitude response. The specimen is perfused with a paramagnetic contrast agent such as Gadolinium or Dysprosium, preferably by bolus injection, after recording one or more baseline images. The phase angle response of the specimen can then be recorded one or more times as the bolus traverses the area of illumination. Fast Fourier transformation converts gradient echo time response data to phase angles for a spatial distribution of volume elements in the illuminated slice. The baseline phase angle image is subtracted from the image taken after the bolus injection, providing a high contrast image showing the distribution of the contrast agent. The change  $\Delta\phi$  in phase angle between the images being generally proportional to the concentration of the contrast agent, the invention enables accurate measurements of localized blood volume and flow rate. The invention is particularly applicable to visualization of cerebral vascular disease causing localized ischemia, such as stroke.

Brief Summary Text (24):

The baseline samples and the data samples can be collected repetitively over a range of different gradient echo parameters, with particular samples or combinations (e.g., averages) of the samples being chosen in order to maximize contrast in the phase angle differences.

Brief Summary Text (25):

A gradient echo sequence of any type can be used, as well as other pulse sequence methods which maintain phase shift in the setting of magnetic field changes (e.g., gradient echo planar, steady state free precession, miscentered RF spin echoes, etc.).

Brief Summary Text (27):

In addition to generating a graphic map, blood volume and blood flow can be quantified absolutely or relatively from the functional relation between phase shift and concentration of the paramagnetic agent in a region of interest in the tissues, or since the phase angle differences  $\Delta\phi$  are generally proportional to the concentration of the paramagnetic contrast agent carried in the blood, relative blood volume and relative blood flow can be quantified.

Drawing Description Text (3):

FIG. 1 is a magnetic resonance display image showing phase shift ( $\Delta\phi$ ) data for a phantom having tubes containing a paramagnetic contrast agent, surrounded by a solution.

Drawing Description Text (4):

FIG. 2a is a graph of phase shift vs. concentration of paramagnetic agent Dy(DTPA) developed from the data shown graphically in FIG. 1.

Drawing Description Text (5):

FIG. 2b is a graph of phase angle per unit of paramagnetic concentration vs. echo time TE, also developed from the data of FIG. 1 and from analogous data collected at different TE values.

Drawing Description Text (6):

FIG. 3a is an image through the basal ganglia of a baboon at 5.1 hours after partial occlusion of the middle cerebral artery, representing the average of a number of phase difference images prepared according to the invention and immediately following bolus contrast agent infusion.

Drawing Description Text (7):

FIG. 3b is an image corresponding to FIG. 3a, showing the spin density weighted signal magnitude image at 5.5 hours after occlusion, a region of eventual infarct being identifiable in the right putamen.

Drawing Description Text (13):

FIG. 5d is a magnitude reconstructed .DELTA.R.sup.\* image (as opposed to phase reconstructed), generated from the same data used to obtain FIG. 5a.

Drawing Description Text (14):

FIG. 6 is a histogram comparing the relative signal to noise ratio of phase difference according to the invention and known magnitude reconstructed .DELTA.R.sup.\* images.

Detailed Description Text (2):

A heterogeneously distributed paramagnetic agent causes a field inhomogeneity resulting in a signal loss in both gradient echo and spin echo magnetic resonance imaging. A paramagnetic agent can also cause a field shift resulting in a net phase shift in a gradient echo, or a miscentered spin echo. Depending on local conditions, paramagnetic contrast agents can be expected to have different effects on signal magnitude and phase angle. For the simple example of a heterogeneous paramagnetic distribution, both a phase shift and signal dephasing would be expected. If the same amount of agent is then homogeneously distributed, only a phase shift would occur. Both the bulk magnetization and the hyperfine coupling effects of contrast agents result in local phase shifts. Locally, the phase shifts are linearly proportional to the contrast agent concentration.

Detailed Description Text (3):

Just as nuclear magnetization is induced when a tissue sample is placed in a magnetic field, an electron magnetization is also induced by a paramagnetic sample placed in a magnetic field, or more precisely, a magnetic induction  $B_{\text{sub}0}$  according to:

Detailed Description Text (8):

where  $T_{\text{sub}E}$  is the time in seconds between an RF pulse and the gradient echo, and P is the "phase activity" which is a property of the paramagnetic agent and the paramagnetic compartment geometry and orientation. For Gadolinium ("Gd(DTPA)"), an additional term is needed due to the susceptibility of the added cation according to Wiedemann's law of additivity. However, the cation diamagnetic susceptibility is at least three orders of magnitude smaller than the paramagnetic susceptibility of the Gd ion, and can be ignored. The underlying diamagnetism of the paramagnetic ion is also small and can be ignored. For a cylindrical paramagnetic compartment oriented perpendicular to the external field and surrounded by a diamagnetic medium, factor  $F = -1/6$  as determined by a surface integral around the cylinder including the effects of the sphere of Lorentz.

Detailed Description Text (11):

In addition to the macroscopic effect of the bulk electron magnetization M on the nuclear spin, an additional microscopic magnetic interaction may be caused by the coordination complex between water and the paramagnetic ion. For nuclear and electron spin angular momentum vectors I and S, and a hyperfine coupling tensor A, the hyperfine interaction is given by  $I \cdot A \cdot S$ , from which a frequency shift can be derived. Because ions in solution tumble rapidly relative to the proton Larmor frequency, the directionality of hyperfine coupling is averaged and the coupling is given by  $AI \cdot S$ , where A is the scalar hyperfine coupling constant. For paramagnetic ions, the hyperfine coupling is modeled as a Fermi contact interaction between the coordinated water and the ion, which causes the protons of complexed water to experience an accelerated Larmor frequency  $\omega_{\text{sub}M}$ . In paramagnetic solutions where the residence time  $\tau_{\text{sub}M}$  of the water complexed to the paramagnetic ion is short compared to  $\omega_{\text{sub}M}^{-1}$ , the hyperfine phase shift can be derived to be:  $\frac{C_{\text{sub}water}}{C_{\text{sub}M}}$  where the water concentration is  $C_{\text{sub}water} = 55M$  and there is one water coordination site per ion. Hyperfine shifts for water coordinated to free unchelated transition metals are known to be relatively small.

Detailed Description Text (12):

For a bolus injection of paramagnetic agent into a peripheral intravenous line, the magnetization M in Equation [1] is established immediately upon passage of the bolus into the magnet bore because the electron  $T_{\text{sub}1}$  is in the microsecond range. As the bolus distributes into the cerebral microvasculature, the paramagnetic concentration  $C_{\text{sub}p}$  (see Equation [4]) will vary with vector position r within the

voxel. The paramagnetic "compartment" in this case can be considered to be the microscopic intravascular space. Alternatively, the paramagnetic compartment can be considered on a more macroscopic scale, e.g., as the grey matter, in which there is a heterogeneous concentration distribution due to vascular compartmentation. Analysis of the magnetization in the latter macroscopic compartment model would involve both a surface integral over the grey matter border and a volume integral over the internal heterogeneity. In experimental data, no significant detectable macroscopic field perturbations have been found in non-perfused tissues adjacent to perfused tissues. Therefore, the former microscopic model treating the intravascular space as the compartment is used as a first approximation. The factor  $F$  (in Equation [4]) may then vary with location  $r$ , depending on vessel shape and connectivity.

Detailed Description Text (15):

where the regional cerebral blood volume  $rCBV = V_{sub. \text{vasc}} / V_{sub. \text{vox}}$  and  $F_{sub. \text{vasc}}$  is the average factor  $F$  for the vascular compartment. The cerebral capillary  $rCBV$  is only about 2% of the tissue volume, and the total intravascular  $rCBV$  is about 4%. The product  $rCBV \cdot C_{sub. \text{vasc}}$  is equivalent to the tissue concentration  $C_{sub. \text{tissue}}$ . If the concentration is not equilibrated within the intravascular space of the voxel, phase shifts would be better represented by the full integral in Equation [8]. It is also possible that the intravascular voxel system can be described by a single factor  $F$ , such as might occur for a continuous, interconnected, patent capillary bed. In this case,  $\Delta \phi_{sub. \text{vox}} \approx 4 \tau \omega_{sub. 0} \chi_{sub. M} T_{sub. E} C_{sub. \text{vasc}} F rCBV$  from Equation [8], where  $C_{sub. \text{vasc}}$  is the average concentration within the vasculature.

Detailed Description Text (17):

The foregoing discussion presents a number of possibilities whereby introducing an exogenous contrast agent and mapping the detected phase angle of an array of volume elements in an RF illuminated slice can result in useful information. This information includes but is not limited to detecting the presence of vascular diseases that are detectable by revealing differences in magnetic susceptibility between adjacent perfused tissues. For example, local blood volumes and flow conditions can be assessed from the reflection of these parameters in the phase angle data collected.

Detailed Description Text (18):

A number of examples of experiments demonstrating application of the invention follow. In a first test, magnetic resonance imaging was applied to a phantom or inanimate test structure in order to quantify and compare the effect of contrast agent concentration on the theoretical bases discussed above. In additional tests, images were collected in vivo from experimental animals. For all experiments, either Gd(DPTA) (available from Berlex, Wayne N.J.) or Dy(DTPA-BMA) (Salutar, Inc., Sunnyvale Calif.) were used as contrast agents.

Detailed Description Text (19):

A phantom containing various concentrations of both agents was made to measure effects of concentration on phase shift. Test tubes (11 mm I.D.; 13 mm O.D.; 54 mm length) were oriented vertically by gluing the base of the tubes to a plastic basin. The test tubes and basin were filled with a 0.2 mM  $MnCl_{sub. 2}$  solution chosen because the  $T_{sub. 1}$  and  $T_{sub. 2}$  values approximate those of brain matter, and the solute is relatively resistant to oxidation-reduction reactions. The phantom was imaged at 19.3 degree C. using a Signa superconducting 1.5 T system (General Electric, Milwaukee Wis.) using a coronal gradient echo sequence at a variety of  $T_{sub. E}$  intervals. The phantom was withdrawn and stock paramagnetic contrast agent solutions were injected into the appropriate tubes to produce concentrations ranging from 0.2 to 4.0 mM. Air bubbles were removed, the phantom was advanced to the position of the previous imaging and post-contrast data were acquired using the same transmitter, receiver and shim settings as the pre-contrast data. From the slope of the phase shift vs. concentration and  $T_{sub. E}$ , the phase activity was measured and applied according to Equation [4] above to extract the factor  $\chi_{sub. M}$ , assuming no hyperfine contribution and using  $F = -1/6$  as appropriate for a cylindrical tube orthogonal to the incident field  $B_{sub. 0}$ . Whereas phase subtraction was used, the analysis is valid even for paramagnetic material outside the sample tube.

Detailed Description Text (20):

Use of the invention for imaging biological tissues was also undertaken to demonstrate its effectiveness, using three baboons. Magnetic resonance images were obtained through the basal ganglia of two of the baboons after unilateral partial middle cerebral artery occlusion using a 2.7-French microcatheter (900  $\mu\text{m}$  O.D.).



The experiment was intended to simulate aspects of a stroke in humans, and protocol approval was obtained from the Johns Hopkins Institutional Review Board.

Detailed Description Text (21):

In the first animal, 0.6 mmol/kg of 500 mM Dy(DTPA-BMA) was bolus injected 5.1 hours after partial occlusion. In the second animal, 0.3 mmol/kg of 500 mM Gd(DTPA) was bolus injected 1.4 hours after partial occlusion. In a third baboon, 0.3 mmol/kg of 500 mM Gd(DTPA) was bolus injected after complete occlusion of the middle cerebral artery and anterior cerebral artery attained by endovascular injection of N-butyl cyanoacrylate adhesive.

Detailed Description Text (23):

The animals were positioned such that a slice normal to the incident field B.sub.0 provided an anatomic coronal image. The same gradient echo sequence was used as in the phantom study, with a T.sub.R /T.sub.E of 33/22 in milliseconds, .alpha.=20.degree., no signal averaging, a 256.times.128 matrix (4.5 sec/image), a 1 cm slice thickness, and a 24 cm field of view (0.9.times.1.9 mm voxels). Flow compensation gradients were not used.

Detailed Description Text (25):

Individual phase angle images were reconstructed on a Sun-4/Sparcstation computer network by zero-filling the raw data to 256 points before performing a two dimensional fast Fourier transform. Baseline phase shifts occur in the absence of paramagnetic agent due to off-resonance effects, eddy currents, static and RF field inhomogeneity, flow along imaging gradients, chemical shift, natural brain paramagnetic content, echo miscentering and other factors, preventing direct measurement of the phase shift .DELTA..phi. from the N individual phase angle images. To correct for these effects, .DELTA..phi. images were generated according to .DELTA..phi..sub.n-1 =arg(Z.sub.n-1), where Z.sub.n-1 =Z.sub.n /Z.sub.1 with Z.sub.n being the complex signal for the n-th image acquisition and Z.sub.1 the signal for the first pre-contrast acquisition. Complex signals were regenerated from the individual phase angle images assuming unit magnitude. This complex arithmetic approach is known for field inhomogeneity mapping (See, Weisskoff, R. M. and Kiihne, S., Magn. Reson. Med. 24, 375-383 (1992) and Yeung, H. M. and Kormos, D. W., Radiology 159, 783-786 (1986)), and also for velocity imaging (Conturo, T. E. and Robinson, B. H., Magn. Reson. Med. 25, 233-247 (1992)). The technique produces robust phase correction. The average phase shift for the imaging series was calculated as .DELTA..phi.=.SIGMA..sub.i=1.sup.N-1 .DELTA..phi..sub.i / (N-1). i/(N-1). If several baseline acquisitions are made and averaged (e.g., to improve signal to noise ratio), the average precontrast phase should be calculated as .phi..sub.pre =argZ.sub.pre, where Z.sub.pre =.SIGMA..sub.i=1.sup.M Z.sub.i /M, and there are M precontrast acquisitions. The average phase calculation from the average complex signal is not previously known. The average baseline phase is calculated in this manner to prevent cancellation artifacts that would occur in the latter case due to slight positional shifts in any borders of phase wraparound. For comparison with the collected phase data, .DELTA.R.sup.\*magnitude images were also extracted, using .DELTA.R.sup.\*.sub.n-1 =-ln(I.sub.n /I.sub.1)/T.sub.E, where I is the signal magnitude.

Detailed Description Text (26):

The images collected are shown by the photographs in FIGS. 1, 3a-3b and 5a-5d. The -.DELTA..phi. image for the phantom is shown in FIG. 1a, where the negative phase shift is shown such that the solutions in the tubes (having a higher paramagnetic concentration) appear bright. The phase shift in the tube is assigned as negative as it is known that the field change in the .+-.Z direction outside the sample tube should be positive. The resulting calibration curve relating phase shift to concentration of paramagnetic contrast agent as shown in FIG. 2a is generally linear, with deviations from linearity apparently caused by field effects from adjacent tubes. The variation in slope as a function of T.sub.E as shown in FIG. 2b represents the phase activity which is described mathematically in Equation [4] above.

Detailed Description Text (27):

From the phase activity as shown, the molar susceptibility .chi..sub.M is calculated from Equation [4] to be 4.5.times.10.sup.-2 cm.sup.3 /mol, which is consistent with the value of 4.8.times.10.sup.-2 cm.sup.3 /mol reported in the literature and also as calculated from Equation [5] at 19.3.degree. C. These results suggest that the bulk susceptibility effect dominates the effect of hyperfine coupling in the application of contrast agents to phase imaging.



Detailed Description Text (28):

The field perturbations that occur around the tubes result in field gradients, which would presumably also occur around capillaries. These gradients are one of the sources of signal loss in magnitude images, due to dephasing and other effects as mentioned above. The extra-compartmental fields average to zero for simple geometries (See FIG. 1a) and might also be expected to average to zero around more complex compartments such as capillaries. As it can be shown that the phase angle samples the average field under certain conditions, the extra-compartmental fields thus do not confuse the image by causing additional phase shift.

Detailed Description Text (29):

For the partial occlusion study using bolus injected Dy(DTPA-BMA) in baboons, individual phase angle images were collected prior to injecting the contrast agent. These phase angle images have significant baseline phase errors including focal phase shifts in the basal ganglia due to iron content. It is possible to correct for baseline phase inhomogeneities by phase subtraction. The subtracted phase is zero within the image noise. FIG. 3a shows the average of all the subsequent baseline-corrected difference images recorded after the bolus had distributed throughout the brain. The phase shift in perfused tissues is positive as verified by imaging phantoms using the same pulse sequence and imaging plane. The subsequent subtracted images provided high spatial resolution and are characterized by anatomically correct grey and white matter differentiation. FIG. 3b is a spin density weighted image which compares closely with the results of the quite clear baseline-corrected average phase angle map of FIG. 3a.

Detailed Description Text (30):

Referring to FIG. 3a, the images recorded show a decreased phase shift in the right putamen, which is ischemic due to the occlusion of cerebral blood circulation. Along the surface of the brain, the phase shift was especially high, which is believed to be due to leptomeningeal/surface cortical circulation. High phase shifts also occur in the regions of the third and lateral ventricles, indicating probable choroid plexus.

Detailed Description Text (31):

The general contrast was reproducibly seen in images recorded for the two other baboons, as discussed below. The maximum observed putamen phase shift of 65.degree. that occurred during the first pass of the contrast bolus corresponds to a frequency shift of 8 Hz or 0.12 ppm, which is much less than the fat/water chemical shift of 235 Hz and is well within the bandwidth of the RF pulse (>1 kHz).

Detailed Description Text (32):

The apparent preservation of resolution in FIG. 3a indicates that resolution was not significantly degraded by macroscopic field gradients between adjacent tissues. The high resolution also indicates that resolution is not significantly affected by changes in concentration and phase that occur during the time in which the respective images are acquired. For a linear concentration change between phase-encoding steps, the reconstructed phase for each pixel will be the average of the phase during the image acquisition. A linear concentration change is assumed, which will best be true in the case of rapid acquisitions and for images acquired during the falling phase of the concentration-time curve. A linear concentration change would also be expected to cause small misregistration along the phase-encoding direction, as occurs in flow misregistration artifacts. If the contrast-induced phase shift accumulated during the k-space acquisition is  $2\pi$ , the signal will be misregistered by one pixel width. If the phase shift is not linear, the effect on the image is a convolution of the Fourier transform of the concentration-time curve and the uncontrasted image, the result of which may be a blurring of the image. In these experiments the maximum linear misregistration artifact in grey and white matter is predicted to be much less than a pixel width because the largest phase shift between successive images was about 35.degree. (see below).

Detailed Description Text (33):

Quantitative region of interest (ROI) data from the ischemic and normal putamena were obtained from the individual .DELTA..phi. images (FIGS. 4a and 4b). The ROI's were located to avoid any macroscopic field gradients that might occur around large vessels. The .DELTA..phi. curves appear to approximate what would be expected for a concentration-time curve. The effects of recirculation of the bolus are clearly demonstrated by peaks that occur every 23 seconds, which is on the order of a mean

body recirculation time of 32 seconds expected for a baboon (calculated from a nominal total blood volume of 8-10% of body weight, and a cardiac output of 0.19 L/min/kg). The difference between the observed and calculated recirculation times may be due to the relatively high heart rate in the test subject (180 BPM) compared to nominal (130-160 BPM), or differences in the transit times of the cerebral and extra-cerebral circulation.

Detailed Description Text (35):

The corrected phase mapping data can be used to produce an image of relative regional cerebral blood volume (rCBV) for comparative analysis. Assuming that a linear relation between .DELTA..phi. and tissue concentration exists (as represented by Equation [10] and reflected by the phantom data), the integral of the phase-time curve of FIG. 4a is proportional to local tissue blood volume as in tracer kinetic analysis. Curve-fitting of the first peak in the curve is not needed for two reasons: first, inasmuch as the phase-time curve in FIG. 4a includes data from several recirculations, the primary and recirculation decay curves are completely sampled and averaged. The area under the curves in FIG. 4a thus represents the weighted-average relative rCBV for the primary and recirculation passes, with very small errors caused by incomplete sampling of the small late recirculation curves. Secondly, regional cerebral blood flow (rCBF) was not calculated, and thus the relationship between the shapes of the input function and the first peak-decay curve need not be assessed. The relative integral values were obtained using ROI's of the averaged .DELTA..phi. image in FIG. 3b, which estimates that the ischemic putamenal blood volume was reduced by 32.7% relative to the contralateral putamen. This measurement is in excellent agreement with the 33% rCBV reduction determined from the ratio curves. These data also suggest that the tissue phase shift is approximately linear with respect to concentration. For example, if the phase shift were quadratically related to concentration, the least squares fit in FIG. 4b would slope upward and the area under the curves in FIG. 4a would indicate a much greater reduction in rCBV compared to that estimated from the latter portion of the ratio curve in FIG. 4b. For comparison, the rCBF measured in the ischemic putamen was reduced by 50% relative to the contralateral putamen as determined from relative putamen microsphere counts obtained after sacrifice. The ischemic putamenal region seen in the image subsequently exhibited a spin density-weighted signal change at a later time (FIG. 3c). The calculated 33% reduction in rCBV is consistent with the measured 50% rCBF reduction as it is known that rCBV is increased in low-grade ischemia as a compensatory mechanism to maintain rCBF. For higher grades of ischemia, this compensatory capacity is exhausted and both rCBV and rCBF fall, although the relative decrease in rCBF from normal levels characteristically exceeds that of the rCBV decrease due to relative vasodilatation and elevated mean transit time (MTT), where  $MTT = rCBV / rCBF$ .

Detailed Description Text (37):

In the second experiment using Gd(DTPA), the .DELTA..phi..sub.5-1 image in the series showed a significant (.about.65%) reduction in phase shift in the acutely ischemic caudate nucleus relative to the normal side (see FIG. 5a). This was the only image in the series which demonstrated significant phase shifts in normal grey and white matter, so blood volumes were not estimated. The phase shifts in FIG. 5a were generally about 25.degree. in the basal ganglia grey matter and about 150.degree. at the cortical surface, and image contrast correlates with that of the spin density weighted image acquired at the same location (FIG. 5b). A spin density-weighted signal abnormality later occurred in the slice immediately adjacent to the region of reduced caudate phase (FIG. 5c).

Detailed Description Text (38):

In the third experiment involving complete middle and anterior cerebral artery occlusion with N-butyl cyanoacrylate adhesive, the phase shift of the involved hemisphere was uniformly zero within phase noise indicating absence of perfusion. This result was later verified by the microspheres. The ipsilateral phase was zero even in regions immediately adjacent to the perfused hemisphere (image not shown), suggesting that the bulk magnetization of perfused tissues does not cause significant field perturbations in surrounding tissues. In all three experiments, the areas of blood volume reduction seen on the .DELTA..phi. images progressed to histologically-proven infarction.

Detailed Description Text (39):

For evaluation of the relative signal-to-noise ratio (SNR), images were magnitude-reconstructed and the change in transverse decay rate (.DELTA.R.sup.\*) was calculated. In the second animal, the ischemic caudate nucleus does not appear

abnormal in the .DELTA.R.sup.\*.sub.5-1 image (FIG. 5d) compared to the .DELTA..phi..sub.5-1 image (FIG. 5a). The relative SNR ratio for the .DELTA..phi. and .DELTA.R.sup.\* methods was calculated on a pixel-by-pixel basis from the averaged images in the first experiment (FIG. 3a) using theoretical signal to noise expressions derived in terms of the pre- and post-contrast signal intensities. A histogram was obtained from a whole brain ROI of the resulting "relative SNR" image and is shown in FIG. 6. The histogram indicates that, on the average, the methods have nearly equivalent SNR, with  $\text{SNR.sub.DELTA..phi.} / \text{SNR.sub.DELTA.R*} = 0.85$ . A relative SNR histogram was also obtained for the 2-1 image which had a mean  $\text{SNR.sub.DELTA..phi.} / \text{SNR.sub.DELTA.R*} = 32.091$ . Accounting for the signal averaging in the averaged images, the histogram width in FIG. 6 is nearly five times as wide as that expected from the width of the 2-1 histogram alone, indicating the presence of significant systematic variation in the relative SNR and thus in the .DELTA..phi. and .DELTA.R.sup.\* values themselves. For example, the .DELTA..phi. method had a higher SNR in the superficial cortex/leptomeninges and in the regions of the choroid plexus, as is apparent from comparing FIGS. 5a and 5d. The absolute noise in the .DELTA..phi. image was measured to be 1.4.degree. using a region of interest of a noncontrast .DELTA..phi. image in which baseline phase shifts were corrected. The maximum grey matter SNR was about 60.degree./1.4.degree. or about 40:1. The relative rCBV determined from the average grey matter .DELTA..phi. of 22.3.degree. for the twenty two data points in FIG. 4a has an SNR or  $\sqrt{22.} (22.3.\text{degree.}) / 1.4.\text{degree.}$  or about 75:1. There were some very small regions of wraparound (e.g., lateral Sylvian fissures), where the maximum SNR was 180.degree./1.4.degree. or about 130:1 for an individual image. As the mean SNR of the two methods is similar, the relative contrast to noise (CNR) of the methods is dependent on the variation in .DELTA..phi. and .DELTA.R\* between different tissues.

#### Detailed Description Text (40):

The invention demonstrates the value of imaging the phase-enhancement effects of bolus-injected paramagnetic contrast agents in the brain. Phase shifts were dynamically acquired and curves of tissue phase response to bolus injection approximate time-activity curves. Images have high tissue contrast and spatial resolution, and large phase shifts can be detected despite small cerebral blood volumes (about 4%). The effects of the initial bolus passage, recirculation, and slow equilibration into the peripheral extracellular fluid are manifest in the collected data. The phase shift as predicted was generally proportional to the tissue concentration, as shown in the phase response curves. Integration of the phase response curves provides a reasonable estimate of relative rCBV in normal grey and white matter and in acutely ischemic grey matter. The SNR in the rCBV image was about 75:1 in the normal grey matter and was comparable to that obtained from magnitude images, although there were some systematic differences in the two methods.

#### Detailed Description Text (42):

Furthermore, the invention can be used to assess magnetic field changes in intrinsic blood or intrinsic tissue such as due to hemoglobin or tissue oxygenation or oxidation states. For example, data can be acquired at identical settings before and during or after visual or other sensory stimulus, execution of a motor task, execution of a cognitive task, or an intervention such as radiation therapy or balloon angioplasty.

#### Detailed Description Text (43):

FIG. 7 illustrates the apparatus of the invention. A source 12 provides a pulsed radio frequency signal for illumination of a patient 14 or other specimen along at least one plane or arbitrary volume traversing the specimen, in the presence of a magnetic field produced by field generator 16. A receiver 18 is responsive to the signal emitted by the specimen, which is of course modulated by the physical characteristics of the specimen, and more particularly by the magnetic properties of the volume elements or voxels of arbitrary size, which are traversed by the plane through the specimen. Sampling means comprising mixing the emitted signal with the signal driving the RF source 12, followed by analog to digital conversion via means 20 and computer processing means 22 acquire a plurality of numeric data samples representing an electromagnetic response of the specimen to the pulsed radio frequency signal. The collected samples can represent, for example, a magnetic resonance spin echo pulse sequence response of the specimen, a steady state free precession pulse sequence response, an echo planar spatial encoding pulse sequence, or a hybrid of one or more of these parameters, in each case including information necessary for obtaining a phase map of the voxels.

Detailed Description Text (44):

The computer 22 is coupled to a memory 32 and is operable to store at least two sets of the data samples corresponding to successive responses of the specimen to the pulsed radio frequency signal. A Fourier transform means 34, which can be a programmed function of computer 22 or an operation effected by an associated processor dedicated to performing fast Fourier transforms, is operable to convert the data samples to a map of phase angles representing a phase response of individual volume elements in the plane to the pulsed radio frequency signal. Computer 22 is operable to subtract the phase response of the individual volume elements in a first of the two sets from a second of the two sets. The results are shown on an output device preferably including a display 16, for example a CRT. It is possible to display the results as a digital on/off presentation of pixels corresponding to the voxels in the illuminated slice through the specimen, for example showing the voxels having a phase angle or phase difference in a certain range. Preferably, however, a phase difference map is displayed wherein at least one of grey levels, brightness, color or the like represent the values for each voxel.

Detailed Description Text (45):

The device may be used to obtain phase angle and phase difference measurements which occur with variations in a physiologic aspect of blood or tissue in the specimen, which variation have characteristic magnetic responses. For example, oxygenation and oxidation characteristics of the blood or tissue produce such variations, and can be perturbed by devices 42 which produce sensory stimulation, modulate motor functions, irradiate tissues with X-rays, heat, light, ultrasound or other irradiations, or mechanically alter blood passages, such as by using angioplasty balloons. Preferably, means 40 for perfusing the specimen are provided for introducing an agent effective to alter a magnetic property of the specimen. Alteration means 40, 42, or both, are effected between acquisition of the two sets of data samples, and in the case of means 40 preferably use either an agent comprising a paramagnetic contrast agent or an agent which alters a physiologic characteristic of blood leading to a difference in magnetic response. This is quite effective when the means for perfusing comprises a bolus injection means which can be regulated by a mechanical regulating device 44, operable to infuse a quantity of the paramagnetic contrast agent at a prescribed rate, into a vascular passage of the specimen. In addition, means 46 for sampling the blood during image acquisition can provide blood concentrations, which enable better assessment of absolute rCBV and rCBF.

Detailed Description Text (46):

Input or control means 50 allow the operator to control computer 22 for selecting alternative presentations for the graphic representation, whereby contrast can be maximized. Alternatively, the computer 22 can be programmed to prepare a variety of different maps, e.g., by selecting among subsets of a plurality of collected images and/or averages of the images to find one or more which have optimal contrast. Computer 22 can also be programmed to compute phase difference maps as outlined herein for any arbitrary pair of data acquisitions.

Detailed Description Text (47):

Triggering means 55 are provided to initiate collection of data samples. The triggering means or the computer 22 or input means 50 can include manually operable means whereby the operator can initiate, pause or terminate collection of a data sample. Timing means can be employed, e.g., as a function of computer 22, to repetitively collect a series of samples after a data collection operation begins. Preferably, the triggering means 55 include a sensor 57 coupled to the specimen and operable to initiate collection of an image at a predetermined time, whereby motion and artifacts in the map are reduced, or temporal registration between data collection and operation of the stimulating device(s) 42 is improved. The triggering means may comprise a cardiac gating trigger operable to initiate collection of the image at a predetermined point in a cardiac cycle of the specimen, or the cardiac gating trigger can be stored for retrospective computer processing.

Detailed Description Text (48):

The specific sampling technique for obtaining the spin echo or gradient echo response of voxels in the specimen can be as disclosed in detail in U.S. Pat. No. 4,766,381--Conturo et al, which is hereby incorporated. According to this technique, during an initial echo period three RF pulses are imposed on the main magnetic field with the first and third pulses rotating the magnetization by a first value (e.g., 90.degree.) and the second pulse having a different value which may be larger than the first (e.g., double or 180.degree.). An echo is created with the second pulse, and the third pulse converts this echo into negative longitudinal magnetization.

After an inversion period and during a second echo period which follows, fourth and fifth RF pulses are applied to the specimen in the main field, thereby creating a spin echo with the fifth pulse. The pulses are all preferably applied with an oscillating field generally perpendicular to the main magnetic field.

Detailed Description Text (50):

The X axis can be employed as the frequency encoding axis from which signals relating to the high and low frequency portions may be provided in composite form. Through Fourier transformation the signals are converted into a map of amplitude versus frequency. This permits correlation between the X coordinate of the signal and the frequency to be established. Similarly, the Y axis can be the phase encoding axis. The varying moments under the influence of the Y axis gradient can be employed to determine differences in gradient-induced phase oscillations between the high field region of the Y gradient and the low field region of the Y gradient. Fourier transformation will provide the distribution of phase oscillation frequencies which can be related to positions along the Y axis. The spin echo signal emitted by the specimen is digitized, and processed as discussed above. Further data acquisitions follow to permit phase difference measurements before and after perfusion, and the phase results are displayed.

Detailed Description Text (51):

The foregoing examples describe particular reconstruction strategies relying on phase shifts. It should be recognized that the presence of phase shifts can be assessed by other reconstruction strategies in which the resulting image brightness is related to the phase shift. Such reconstructions include phase-sensitive reconstruction with display of either the real or imaginary portions of the complex signal intensity (2) or (2) with or without correction for baseline phase errors (in this case, there is a one to one correspondence between real image brightness and phase angles for phase angles ranging from zero to  $2\pi$ ). Other reconstructions which can monitor phase shifts include computation of the magnitude of the complex signal difference generated by complex number subtraction of, e.g., the n-th and first images according to  $\text{vertline} \cdot \Delta Z \cdot \text{vertline} = \text{vertline} \cdot (Z_{\text{sub}n} - Z_{\text{sub}1}) \cdot \text{vertline}$ , in which case  $\text{vertline} \cdot \Delta Z \cdot \text{vertline}$  is approximately proportional to  $\Delta \phi$  for very small values of  $\Delta \phi$ . In both these cases the signal to noise will be no greater and will usually be significantly less than that of a true calculated  $\Delta \phi$  image as disclosed. Other calculations such as measurement of  $\Delta \phi$  as  $\Delta \phi = \arg(Z_{\text{sub}n} - Z_{\text{sub}1})$  will only be accurate if the signal magnitudes are equal, i.e., if  $\text{vertline} \cdot Z_{\text{sub}n} \cdot \text{vertline} = \text{vertline} \cdot Z_{\text{sub}1} \cdot \text{vertline}$ , which generally will not be the case due to signal dephasing. In all these alternative reconstructions, the functional linear relation between pixel value (e.g., image brightness) and tissue paramagnetic concentration which is essential for assessment of rCBV and rCBF will not be obeyed. Therefore, the  $\Delta \phi$  reconstruction as presented in the above description is preferred. Nevertheless, the invention is intended to encompass such alternative reconstructions relying on phase.

Detailed Description Text (52):

The invention is particularly applicable to identify cerebral vascular disease. Similar techniques can be used for diagnostic and/or measurement purposes with respect to other aspects of the cerebrum, or aspects of extracerebral brain tissue, the myocardium, spinal cord, kidney, liver, spleen or bowel, pancreas, skeletal muscle, lung or bone marrow, etc.

Other Reference Publication (1):

Wedeen et al., "Projective Imaging of Pulsatile Flow with Magnetic Resonance", 230 Science 946-948 (1985). (no month).

CLAIMS:

1. A method for imaging a specimen comprising one of a substance traversed by passages and a material having a changeable magnetization, comprising the steps of:  
illuminating the specimen along at least one plane traversing the localized area, using a pulsed radio frequency source, and collecting at least one baseline sample representing an electromagnetic response of the specimen to the pulsed radio frequency source;

altering a magnetic property of the specimen by one of perfusing the specimen with an agent having a magnetic property different from a corresponding magnetic property

of the specimen at least in a localized area to be imaged, and physically perturbing the specimen to induce a macroscopic change in the magnetic property;

illuminating the specimen along at least one plane traversing the localized area, using the pulsed radio frequency source;

collecting a plurality of data samples representing the electromagnetic response of the specimen, including the agent, to the pulsed radio frequency source;

converting the data samples into a map of phase information for an array of volume elements in said plane to thereby construct an image from variations in the electromagnetic responses of the volume elements as represented by different shifts in one of frequency, phase, real, imaginary and complex signal information between the source illuminating the specimen and the data samples collected therefrom:

correcting phase angles representing the volume elements in the array to cancel variations that are present in both the data samples and the baseline sample; and,

identifying variations in the localized area by corresponding variations in phase information of the volume elements in said map.

2. The method according to claim 1, comprising collecting a plurality of said samples, and correcting the phase angles of the volume elements in said map by canceling variations which are present in both of two selected subsets of the samples, the subsets respectively including at least one baseline sample taken prior to said altering step, at least one data sample taken after the altering step, selected groups taken from a plurality of data samples and baseline samples, and selected averages including the data samples and baseline samples.

3. The method according to claim 1, wherein the specimen is a biological specimen having tissues traversed by vascular passages, and wherein the altering step includes infusing the specimen with a paramagnetic contrast agent which perfuses the tissues.

4. The method according to claim 2, wherein at least one of the baseline samples and the data samples are collected repetitively over a range of different gradient echo parameters, and further comprising selecting among the baseline and data samples of different gradient echo parameters in order to maximize contrast in the phase angles.

5. The method according to claim 2, wherein the phase differences are produced by multiplying complex signals by a phase factor for at least one of improving signal to noise ratio and reducing wraparound.

6. The method according to claim 5, wherein an average baseline phase is computed from an argument of an average baseline complex signal.

7. The method according to claim 4, wherein the converting step includes performing a Fourier transformation on the samples along a group of gradient echo parameters, for at least one of improving a signal-to-noise ratio of the samples, minimizing phase wraparound, and assessment of intravoxel phase distribution.

8. The method according to claim 3, wherein the altering step comprises bolus-injecting the paramagnetic contrast agent, prior to collecting the data samples.

11. The method according to claim 1, wherein the specimen is a biological specimen having tissues traversed by vascular passages, and wherein the agent includes intrinsic blood having a variation from nominal intrinsic blood in one of an oxygenation level and an oxidation state thereof, said variation being produced by one of a physiologic characteristic of the specimen and an externally induced change.

12. The method according to claim 1, wherein the specimen comprises biological tissue and wherein said perturbation includes at least one of irradiation, application of light application of heat, application of sound, sensory stimulus motor stimulus application of balloon angioplasty, application of pharmacologic agents and execution of a cognitive task.



13. The method according to claim 10, wherein the agent is chosen from the group consisting of diamagnetic, ferromagnetic and superparamagnetic species.
14. The method according to claim 3, wherein the localized area includes cerebral tissue and the passages are vascular structures.
15. The method according to claim 1, wherein the localized area includes tissue of at least one of a cerebrum, extracerebral brain tissue, myocardium, spinal cord, kidney, liver, spleen, bowel, pancreas, skeletal muscle, lung, bone marrow, and connective tissue.
17. The method according to claim 16, wherein the sample comprises cerebral tissue and the passages are vascular structures, and wherein said identifying step includes computer analyzing the map for a localized area of ischemia characterized by localized variations in the phase angles.
18. The method according to claim 16, wherein the sample comprises cerebral tissue and the flow passages are vascular structures including large arteries, veins, arterioles and venules, and small capillaries, and wherein the variations represent at least one of a tumor, infection, hematoma, embolism and infarction.
19. The method according to claim 16, wherein the localized area includes tissue of at least one of a cerebrum, extracerebral brain tissue, myocardium, spinal cord, kidney, liver, spleen, bowel, pancreas skeletal muscle, lung, bone marrow, and connective tissue, said identifying step including computer analyzing the map for localized variations in the phase angles characterizing an area of at least one of ischemia, tumor, hematoma, infection, embolism and infarction.
21. An apparatus for magnetic resonance imaging, comprising:
- a source of a pulsed radio frequency signal for illumination of a specimen along at least one plane traversing the specimen;
- sampling means operable to acquire a plurality of data samples representing at least one of an electromagnetic gradient echo response and a spin echo response of the specimen to the pulsed radio frequency signal;
- data processing means operable to store at least two sets of said data samples corresponding to successive responses of the specimen to the pulsed radio frequency signal, the data processing means including a Fourier transform means operable to convert the data samples to complex intensities, and the data processing means converting the complex intensities to a map of phase information representing a phase response of individual volume elements in the plane to the pulsed radio frequency signal through a macroscopic volume of the specimen, and means for correcting the phase response of the individual volume elements in a second of the two sets from a first of the two sets;
- means for altering a magnetic property of the specimen in the macroscopic volume, between acquisition of the two sets; and,
- a display coupled to the data processing means for graphic representation of the phase response of the individual volume elements.
22. The apparatus according to claim 21, further comprising triggering means coupled to the source and the sampling means, the triggering means being operable for at least one of monitoring physiologic signals from the specimen, initiating external stimuli of the specimen, and triggering the source and the sampling means respectively to illuminate the specimen and to collect the data samples.
23. The apparatus according to claim 21, wherein the data processor is operable to process said data samples for quantification of at least one of rCBV, rCBF, and MTT.
25. The apparatus according to claim 21, further comprising means coupled to the specimen for blood sampling in connection with data acquisition.
28. The apparatus according to claim 21, wherein the sampling means and the data processing means are operable in conjunction to acquire a plurality of successive responses of the specimen at different gradient echo parameters, and further

comprising means for selecting alternative presentations for said graphic representation, whereby contrast can be maximized.

29. The apparatus according to claim 28, wherein the data processing means is operable to compute a baseline phase map from an argument of an average baseline complex signal calculated from a plurality of baseline data acquisitions.

30. The apparatus according to claim 21, wherein the sampling means is operable to encode a magnetic resonance spin echo pulse sequence response of the specimen.

34. The apparatus according to claim 33, wherein the triggering means comprises a cardiorespiratory gating trigger operable for at least one of initiating collection of the image at a predetermined point in a cardiorespiratory cycle, providing cardiorespiratory data for retrospective processing of the data samples, initiating application of an external stimulus to the specimen, and enabling an external triggering means to initiate data acquisition.

35. The apparatus according to claim 22, wherein the triggering means is operable to effect at least one of EKG tracking, respiratory monitoring, EEG tracking and triggering of additional magnetic resonance imaging signals for at least one of reducing motion artifacts and collection of an image at least at one predetermined point in cardiac and respiratory cycles of the specimen.



## End of Result Set



Generate Collection

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L13: Entry 10 of 10

File: USPT

Jul 13, 1993

DOCUMENT-IDENTIFIER: US 5226418 A

TITLE: Phase correction of complex - difference processed magnetic resonance angiogramsAbstract Text (1):

An NMR system produces an angiogram using the complex-difference method. Artifacts caused by system phase errors are reduced by calculating a corrected phase angle using the acquired NMR data sets and using the corrected phase angle in calculating the complex difference in the corresponding elements of the image domain NMR data sets.

Brief Summary Text (2):

The field of the invention is nuclear magnetic resonance imaging methods and systems. More particularly, the invention relates to magnetic resonance angiograms which are produced using complex differences between image data sets acquired with different values of gradient field first moments.

Brief Summary Text (4):

When a substance such as human tissue is subjected to a uniform magnetic field (polarizing field  $B_{sub.0}$ ), the individual magnetic moments of the spins in the tissue attempt to align with this polarizing field, but precess about it in random order at their characteristic Larmor frequency. A net magnetic moment  $M_{sub.z}$  is produced in the direction of the polarizing field, but the randomly oriented magnetic components in the perpendicular, or transverse, plane (x-y plane) cancel one another. If, however, the substance, or tissue, is subjected to a magnetic field (excitation field  $B_{sub.1}$ ) which is in the x-y plane and which is near the Larmor frequency, the net aligned moment,  $M_{sub.z}$ , may be rotated, or "tipped", into the x-y plane to produce a net transverse magnetic moment  $M_{sub.t}$ , which is rotating, or spinning, in the x-y plane at the Larmor frequency. The degree to which the net magnetic moment  $M_{sub.z}$  is tipped (flip angle), and hence the magnitude of the net transverse magnetic moment  $M_{sub.t}$  depends primarily on the length of time and the magnitude of the applied excitation field  $B_{sub.1}$ .

Brief Summary Text (7):

Another important factor which contributes to the amplitude A of the NMR signal is referred to as the spin-lattice relaxation process which is characterized by the time constant  $T_{sub.1}$ . It describes the recovery of the net magnetic moment M to its equilibrium value along the axis of magnetic polarization (z). The  $T_{sub.1}$  time constant is longer than  $T_{sub.2}$ , much longer in most substances of medical interest.

Brief Summary Text (8):

The NMR measurements of particular relevance to the present invention are called "pulsed NMR measurements". Such NMR measurements are divided into a period of RF excitation and a period of signal emission. Such measurements are performed in a cyclic manner in which the NMR measurement is repeated many times to accumulate different data during each cycle or to make the same measurement at different locations in the subject. A wide variety of preparative excitation techniques are known which involve the application of one or more RF excitation pulses ( $B_{sub.1}$ ) of varying magnitude, duration, and direction. Such excitation pulses may have a narrow frequency spectrum (selective excitation pulse), or they may have a broad frequency spectrum (nonselective excitation pulse) which produces transverse magnetization  $M_{sub.t}$  over a range of resonant frequencies. The prior art is replete with excitation techniques that are designed to take advantage of particular NMR

phenomena and which overcome particular problems in the NMR measurement process.

Brief Summary Text (9):

When utilizing NMR to produce images, a technique is employed to obtain NMR signals from specific locations in the subject. Typically, the region which is to be imaged (region of interest) is scanned by a sequence of NMR measurement cycles which vary according to the particular localization method being used. The resulting set of received NMR signals are digitized and processed to reconstruct the image using one of many well known reconstruction techniques. To perform such a scan, it is, of course, necessary to elicit NMR signals from specific locations in the subject. This is accomplished by employing magnetic fields ( $G_{sub.x}$ ,  $G_{sub.y}$ , and  $G_{sub.z}$ ) which have the same direction as the polarizing field  $B_{sub.0}$ , but which have a gradient along the respective x, y and z axes. By controlling the strength of these gradients during each NMR cycle, the spatial distribution of spin excitation can be controlled and the location of the resulting NMR signals can be identified.

Brief Summary Text (10):

NMR data for constructing images can be collected using one of many available techniques. Typically, such techniques comprise a pulse sequence made up of a plurality of sequentially implemented views. Each view may include one or more NMR experiments, each of which comprises at least an RF excitation pulse and a magnetic field gradient pulse to encode spatial information into the resulting NMR signal. As is well known, the NMR signal may be a free induction decay (FID) or a spin-echo signal.

Brief Summary Text (11):

The present invention will be described in detail with reference to a variant of the well known Fourier transform (FT) imaging technique, which is frequently referred to as "spin-warp". The spin-warp technique is discussed in an article entitled "Spin Warp NMR Imaging and Applications to Human Whole-Body Imaging" by W. A. Edelstein et al., Physics in Medicine and Biology, Vol. 25, pp. 751-756 (1980). It employs a variable amplitude phase encoding magnetic field gradient pulse prior to the acquisition of NMR spin-echo signals to phase encode spatial information in the direction of this gradient. In a two-dimensional implementation (2DFT), for example, spatial information is encoded in one direction by applying a phase encoding gradient ( $G_{sub.y}$ ) along that direction, and then a spin-echo signal is acquired in the presence of a readout magnetic field gradient ( $G_{sub.x}$ ) in a direction orthogonal to the phase encoding direction. The readout gradient present during the spin-echo acquisition encodes spatial information in the orthogonal direction. In a typical 2DFT pulse sequence, the magnitude of the phase encoding gradient pulse  $G_{sub.y}$  is incremented ( $\Delta G_{sub.y}$ ) in the sequence of views that are acquired during the scan to produce a set of NMR data from which an entire image can be reconstructed.

Brief Summary Text (12):

There are a number of well known NMR techniques for measuring the motion, or flow of spins within the region of interest. These include the "time-of-flight" method in which a bolus of spins is excited as it flows past a specific upstream location and the state of the resulting transverse magnetization is examined at a downstream location to determine the velocity of the bolus. This method has been used for many years to measure flow in pipes, and in more recent years it has been used to measure blood flow in human limbs. Examples of this method are disclosed in U.S. Pat. Nos. 3,559,044; 3,191,119; 3,419,793 and 4,777,957.

Brief Summary Text (13):

A second flow measurement technique is the inflow/outflow method in which the spins in a single, localized volume or slice are excited and the change in the resulting transverse magnetization is examined a short time later to measure the effects of excited spins that have flowed out of the volume or slice, and the effects of differently excited spins that have flowed into the volume or slice. Examples of this method are described in U.S. Pat. Nos. 4,574,239; 4,532,474 and 4,516,582.

Brief Summary Text (14):

A third technique for measuring motion or flow relies upon the fact that an NMR signal produced by spins flowing through a magnetic field gradient experiences a phase shift which is proportional to velocity. This is referred to in the art as the "phase modulation" technique. For flow that has a roughly constant velocity during the measurement cycle the change in phase of the NMR signal is given as follows:

Brief Summary Text (15):

where  $M_{sub.1}$  is the first moment of the magnetic field gradient,  $\gamma$  is the gyromagnetic ratio and  $v$  is the velocity of the spins. To eliminate errors in this measurement due to phase shifts caused by other sources, it is common practice to perform the measurement at least twice with different magnetic field gradient moments as described in U.S. Pat. No. 4,609,872. The difference in phase at any location between the two measurements is then as follows:

Brief Summary Text (16):

By performing two complete scans with different magnetic field gradient first moments and subtracting the measured phases in the reconstructed image at each location in the acquired data arrays, a phase map is produced which accurately measures the velocity of constantly moving spins.

Brief Summary Text (17):

Magnetic resonance angiograms are produced by acquiring and calculating the phase difference between at least two NMR data sets, each with a different value for the first moment of a magnetic field gradient. The phase is substantially the same in the two data sets at locations where the spins are stationary and such tissues appear dark in the reconstructed image. On the other hand, moving spins impart a phase to the acquired NMR signal which is proportional to velocity and the value of the first moment of the magnetic field gradient. Since the first moments are different in the two acquired NMR data sets, moving spins will produce a phase difference and the locations where these phase differences occur will appear bright in the angiogram image.

Brief Summary Text (18):

There are a number of methods currently used to produce phase difference angiogram data from two or more acquired NMR data sets. In one method, which is referred to as the "phase difference method" the difference in phase between corresponding elements in the acquired NMR images is calculated and this phase difference is used to control the intensity of the corresponding image pixel. In a second method, which is referred to as the "complex difference method", the in-phase and quadrature components of corresponding elements in two acquired NMR raw data sets are subtracted to produce complex difference data which is then Fourier transformed into the image domain. Alternatively and equivalently, the two raw NMR data sets can be Fourier transformed, and the in-phase and quadrature components in corresponding image elements can be subtracted. In any case, the complex difference image is used to reconstruct the angiogram image. There are subtle differences between the angiograms produced by the phase difference and complex difference methods which make them both uniquely useful in clinical applications.

Brief Summary Text (19):

The accurate reconstruction of a magnetic resonance angiogram using either of these processing methods assumes that there are no phase errors in the measurements. While there are many sources of phase errors, most phase errors are the same in the two acquired data sets and are subtracted out of the image data by the difference process. However, some phase errors may be different in the two acquired data sets and the difference process used to produce an angiogram will produce artifacts in the reconstructed image.

Brief Summary Text (20):

There are a number of methods known for correcting phase errors in NMR measurements. For example, Juwhan Liu et al describe a phase correction technique in the Journal of Magnetic Resonance, Vol. 86 pp 593-604 (1990) in an article entitled "An Automatic Phase Correction Method In Nuclear Magnetic Resonance Imaging" which reduce errors due to such system hardware problems as (a) misadjustment of the reference phase relative to the receiver phase detector; (b) phase shifts caused by noise filters; (c) incorrect alignment of data acquisition window; (d) imperfect selective RF excitation pulses; (e) amplifier dead time; and (f) eddy currents. Other phase correction methods are described by C. B. Ahn et al in an article in IEEE Transactions On Medical Imaging, Vol M1-6 No. 1 March 1987 entitled "A New Phase Correction Method In NMR Imaging Based On Autocorrelation And Histogram Analysis"; and by M. A. Bernstein et al in an article in Medical Physics, Vol. 16 No. 5, Sept/Oct 1989 entitled "Improved Detectability In Low Signal-To-Noise Ratio Magnetic resonance Images By Means Of A Phase-Corrected Real Reconstruction". None of these techniques have been employed to correct angiograms produced by the complex difference method.

#### Brief Summary Text (22):

The present invention relates to a method and apparatus for producing NMR angiograms using the image domain complex difference method and for reducing image artifacts in such angiograms due to system phase errors. More particularly, the present invention includes the acquisition of a plurality of NMR k-space data sets using pulse sequences with different magnetic field gradient first moments, Fourier transforming the plurality of k-space data sets to produce a corresponding plurality of image space data sets; calculating the angle between the vector represented by each element in one image space data set and the vector represented by each corresponding element in another of said image space data sets and storing the angles as corresponding elements in a phase difference array; calculating the values in a corrected phase difference array from the corresponding values in the phase difference array; and calculating the values in a difference data set from which an angiogram is produced using the corresponding values in each of said plurality of image space data sets and the corresponding values in the corrected phase difference array.

#### Brief Summary Text (23):

A general object of the invention is to correct phase errors in angiogram NMR data sets which are produced using the complex difference method. A number of methods are known for calculating the value of phase errors from phase difference NMR data. The present invention enables such phase errors to be calculated, and provides a method for applying corrections based on these phase error calculations to the image domain complex difference data used to produce the angiogram.

#### Drawing Description Text (2):

FIG. 1 is a block diagram of an NMR system which employs the present invention;

#### Drawing Description Text (3):

FIG. 2 is an electrical block diagram of the transceiver which forms part of the NMR system of FIG. 1;

#### Drawing Description Text (4):

FIGS. 3A-3C are graphic representations of the NMR pulse sequences used in the preferred embodiments to acquire the NMR data sets employed to reconstruct an angiogram according to the present invention; and

#### Drawing Description Text (5):

FIG. 4 is a pictorial representation of how an angiogram is reconstructed using the NMR data sets acquired with the system of FIG. 1 using the pulse sequence of FIG. 3.

#### Detailed Description Text (2):

Referring first to FIG. 1, there is shown in block diagram form the major components of a preferred NMR system which incorporates the present invention and which is sold by the General Electric Company under the trademark "SIGNA". The overall operation of the system is under the control of a host computer system generally designated 100 which includes a main computer 101 (such as a Data General MV7800). The computer has associated therewith an interface 102 through which a plurality of computer peripheral devices and other NMR system components are coupled. Among the computer peripheral devices is a magnetic tape drive 104 which may be utilized under the direction of the main computer for archiving patient data and images to tape. Processed patient data may also be stored in an image disc storage device designated 110. The function of image processor 108 is to provide interactive image display manipulation such as magnification, image comparison, gray-scale adjustment and real-time data display. The computer system is provided with a means to store raw data (i.e. before image construction) utilizing a disc data storage system designated 112. An operator console 116 is also coupled to the computer by means of interface 102 and provides the operator with the means to input data pertinent to a patient study as well as additional data necessary for proper NMR system operation, such as calibrating, initiating and terminating scans. The operator console is also used to display images stored on discs or magnetic tape.

#### Detailed Description Text (3):

The computer system 100 exercises control over the NMR system by means of system control 118 and gradient amplifier system 128. The computer 100 communicates with system control 118 by means of a link 103 in a manner well known to those skilled in the art. The system control 118 includes several subsystems such as a pulse control module (PCM) 120, an array processor 106, a radio frequency transceiver 122, a

status and control module (SCM) 124, and the power supplies generally designated 126 necessary to energize the components. The PCM 120 utilizes control signals provided by main computer 101 to generate digital timing and control signals such as the digital waveforms which control gradient coil excitation, as well as RF envelope waveforms utilized in the transceiver 122 for modulating the RF excitation pulses. The gradient waveforms are applied to the gradient amplifier system 128 generally comprised of G.sub.x, G.sub.y and G.sub.z amplifiers 130, 132 and 134, respectively. Each amplifier 130, 132 and 134 is utilized to excite a corresponding gradient coil in an assembly generally designated 136. When energized, the gradient coils generate magnetic field gradients G.sub.x, G.sub.y and G.sub.z of the magnetic field in the same direction as the main polarizing magnetic field, wherein the gradients are directed in mutually orthogonal X-, Y- and Z-axis directions of a Cartesian coordinate system. That is, if the magnetic field generated by the main magnet (not shown) is directed in the z direction and is termed B.sub.0, and the total magnetic field in the z direction is referred to as B.sub.z, then  $G_{\text{sub}.x} = \frac{dB_{\text{sub}.z}}{dx}$ ,  $G_{\text{sub}.y} = \frac{dB_{\text{sub}.z}}{dy}$  and  $G_{\text{sub}.z} = \frac{dB_{\text{sub}.z}}{dz}$ , and the magnetic field at any point (x, y, z) is given by  $B(x, y, z) = B_{\text{sub}.0} + G_{\text{sub}.x}x + G_{\text{sub}.y}y + G_{\text{sub}.z}z$ .

Detailed Description Text (4):

The gradient magnetic fields are utilized in combination with radio frequency pulses generated by transceiver 122, RF amp 123 and RF coil 138 to encode spatial information into the NMR signals emanating from the region of the patient being studied. Waveforms and control signals provided by the pulse control module 120 are utilized by the transceiver subsystem 122 for RF carrier modulation and mode control. In the transmit mode, the transmitter provides a radio frequency waveform modulated in accordance with the control signals to an RF power amplifier 123 which then energizes RF coil 138 which is situated within main magnet assembly 146. The NMR signals radiated by the excited nuclei in the patient are sensed by the same or a different RF coil than is used for transmitting and amplified by a preamplifier 139. The NMR signals are amplified, demodulated, filtered, and digitized in the receiver section of the transceiver 122. The processed NMR signals are transmitted to the array processor 106 for processing by means of a dedicated, unidirectional link 105.

Detailed Description Text (6):

The gradient coil assembly 136 and the RF transmit and receiver coils 138 are mounted within the bore of the magnet utilized to produce the polarizing magnetic field. The magnet forms a part of the main magnet assembly which includes the patient alignment system 148. A shim power supply 140 is utilized to energize shim coil associated with the main magnet and which are used to correct inhomogeneities in the polarizing magnetic field. In the case of a resistive magnet, main magnet power supply 142 is utilized to continuously energize the magnet. In the case of a superconductive magnet, the main power supply 142 is utilized to bring the polarizing field produced by the magnet to the proper operating strength and is then disconnected. In the case of a permanent magnet, power supply 142 would not be needed. The patient alignment system 148 operates in combination with a patient cradle and transport system 150 and patient positioning system 152. To minimize interference from external sources, the NMR system components comprised of the main magnet assembly, the gradient coil assembly, and the RF transmit and receiver coils, as well as the patient-handling devices, are enclosed in an RF-shielded room generally designated 144.

Detailed Description Text (7):

Referring particularly to FIGS. 1 and 2, the transceiver 122 includes components which produce the RF excitation field B.sub.1 through power amplifier 123 at a coil 138A and components which receive the resulting NMR signal induced in a coil 138B. The base, or carrier, frequency of the RF excitation field is produced under control of a frequency synthesizer 200 which receives a set of digital signals through the communications link 103 from the main computer 101. These digital signals indicate the frequency and phase of the RF carrier signal which is produced at an output 201. The commanded RF Carrier is applied to a modulator 202 where it is modulated in response to a signal R(t) received through bus 103 from the PCM 120. The signal R(t) defines the envelope, and therefore the bandwidth, of the RF excitation pulse to be produced. It is produced in the PCM 120 by sequentially reading out a series of stored digital values as the RF excitation pulse is produced that represent the desired envelope. These stored digital values may, in turn, be changed by the computer 100 to enable any desired RF pulse envelope to be produced. The magnitude

of the RF excitation pulse output through line 205 is attenuated by a transmit attenuator circuit 206 which receives a digital signal, TA, from the main computer 101 through communications link 103. The attenuated RF excitation pulses are applied to the power amplifier 123 that drives the RF transmitter coil 138A. For a more detailed description of this portion of the transceiver 122, reference is made to U.S. Pat. No. 4,952,877 which is incorporated herein by reference.

Detailed Description Text (8):

Referring still to FIGS. 1 and 2 the NMR signal produced by the subject is picked up by the receiver coil 138B and applied to the input of a receiver 207. The receiver 207 amplifies the NMR signal and this is attenuated by an amount determined by a digital attenuation signal (RA) received from the main computer 101 through link 103. The receiver 207 is also turned on and off by a signal through line 211 from the PCM 120 such that the NMR signal is acquired only over the time intervals required by the particular acquisition being performed.

Detailed Description Text (9):

The received NMR signal is at or around the Larmor frequency, which in the preferred embodiment is around 63.86 MHz. This high frequency signal is demodulated in a two step process in a demodulator 208 which first mixes the NMR signal with the carrier signal on line 201 and then mixes the resulting signal with the 2.5 MHz reference signal on line 204. The resulting demodulated NMR signal on line 212 has a bandwidth of 125 kHz and it is centered at a frequency of 187.5 kHz. The demodulated NMR signal is applied to the input of an analog-to-digital (A/D) converter 209 which samples and digitizes the analog signal at a rate of 250 kHz. The output of the A/D converter 209 is applied to a digital quadrature detector 210 which produces 16-bit in-phase (I) values and 16-bit quadrature (Q) values corresponding to the received digital signal. The resulting stream of digitized I and Q values of the received NMR signal is output through bus 105 to the array processor where they are employed to reconstruct an image.

Detailed Description Text (10):

To preserve the phase information contained in the received NMR signal, both the modulator 202 in the transmitter section and the demodulator 208 in the receiver section are operated with common signals. More particularly, the carrier signal at the output 201 of the frequency synthesizer 200 and the 2.5 MHz reference signal at the output 204 of the reference frequency generator 203 are employed in both the modulation and the demodulation process. Phase consistency is thus maintained and phase changes in the demodulated received NMR signal accurately indicate phase changes produced by the excited spins. The 2.5 MHz reference signal as well as 5, 10 and 60 MHz reference signals are produced by the reference frequency generator 203 from a common 10 MHz clock signal, and the latter three reference signals are employed by the frequency synthesizer 200 to produce the carrier signal on output 201. For a more detailed description of the receiver, reference is made to U.S. Pat. No. 4,992,736 which is incorporated herein by reference.

Detailed Description Text (11):

The NMR system of FIG. 1 performs a series of pulse sequences to collect sufficient NMR data to reconstruct the desired angiogram. Referring particularly to FIG. 3A, the first pulse sequence is a conventional first order moment nulled gradient echo sequence in which a selective RF excitation pulse 300 is applied to the subject in the presence of a G.sub.z slice select gradient pulse 301. The excitation pulse 300 has a flip angle .alpha. with a typical value of .alpha. being 30.degree.. To compensate the FID for the phase shifts caused by the slice select gradient pulse 301 and to desensitize the FID to velocity along the z axis, a negative G.sub.z gradient pulse 304 followed by a positive G.sub.z gradient pulse 305 are produced by the G.sub.z gradient coils. For example, one solution is to use a pulse 304 of the same width, but opposite sign, as the pulse 301, and the pulse 305 is one half the width and the same height as the pulse 301. While the pulses 304 and 305 compensate for velocity along the z axis, more complex gradient waveforms are also well known to those skilled in the art for compensating acceleration and even higher orders of motion.

Detailed Description Text (12):

To position encode the NMR signal 303 a phase encoding G.sub.y gradient pulse 306 is applied to the subject shortly after the application of the RF excitation pulse 300. As is well known in the art, a complete scan is comprised of a series of these pulse sequences in which the value of the G.sub.y phase encoding pulse is stepped through a series of, for example, 256 discrete phase encoding values to locate the position



of the spins producing the NMR signal along the y axis. Position along the x axis is located by a G.sub.x gradient pulse 307 which is produced as the NMR gradient echo signal 303 is acquired and which frequency encodes the NMR signal 303. Unlike the G.sub.y phase encoding gradient pulse 306, the G.sub.x readout gradient pulse 307 remains at a constant value during the entire scan. To produce the gradient echo 303 and to desensitize it to velocity along the x axis, gradient pulses 308 and 309 are produced prior to the pulse 307. There are a number of well known strategies to accomplish this.

Detailed Description Text (13):

As is explained in more detail below, to practice the present invention, at least two complete data sets, each with different flow sensitivity along one direction, are needed. In the preferred embodiment data for the sets is acquired in an interleaved fashion. In this approach, two or more measurements with different flow sensitivity are acquired with one value of the phase encoding gradient. The phase encoding value is then changed and additional measurements are made at this new phase encoding value with the two or more flow sensitivities. This process continues until all the phase encoding values have been employed. The acquired data is then reordered into k-space NMR data sets, each with a different flow sensitivity. While this interleaved approach is preferred because it minimizes effects due to other motion (e.g. respiratory), in the following discussion the invention is described as if the k-space NMR data sets are each completely acquired prior to the next flow encoding being used.

Detailed Description Text (14):

The NMR signal 303 is acquired by the system transceiver 122 and digitized into a row of 256 complex numbers which are stored in the memory of the main computer 101. For each value of the G.sub.y phase encoding gradient an NMR signal 303 is produced, acquired, digitized and stored in a separate row of 256 complex numbers. At the completion of the scan, therefore, a two-dimensional (256.times.256) matrix of complex numbers is stored in the computer 101. If these NMR signals are produced when no flow sensitizing gradients are applied, the k-space NMR data set may be Fourier transformed into a conventional NMR image. This is represented in FIG. 3A by the gradient G.sub.M which is zero when no velocity encoding magnetic field gradient first moment is employed in the pulse sequence.

Detailed Description Text (15):

To produce an angiogram according to the present invention the acquired NMR signals are velocity sensitized. The pulse sequence used is the same as that shown in FIG. 3A, except the gradient G.sub.M now has a value which sensitizes the acquired NMR signals to velocity along the direction of G.sub.M. This is illustrated in FIG. 3B, where G.sub.M has a bipolar waveform comprised of a negative gradient pulse 310 followed by a positive gradient pulse 311. The area (A) defined by each pulse 310 and 311 is the same, and the centers of each gradient pulse 310 and 311 are spaced from one another by a time interval (t). The incremental first moment (.DELTA.M.sub.1) provided by the G.sub.M gradient is, therefore .DELTA.M.sub.1 = A.times.t, and this gradient first moment .DELTA.M.sub.1 is applied after the application of the RF excitation pulse 300 and before the acquisition of the signal 303. While the gradient G.sub.m is illustrated as a separate gradient magnetic field, in fact, it is produced by the same coils which produce the G.sub.x, G.sub.y and G.sub.z gradient fields. By combining G.sub.x, G.sub.y and G.sub.z gradient fields of the proper amplitude, the gradient moment G.sub.M can be oriented in any direction in space in order to sensitize for flow in that direction. For example, it is quite common to sensitize for flow in the slice selection direction, in which case the gradient moment G.sub.M is produced solely by the G.sub.z gradient coil. Thus, in the preferred embodiment a first array of NMR raw signals Z.sub.1 is acquired using the pulse sequence of FIG. 3A, but with the G.sub.M gradient field of FIG. 3B added.

Detailed Description Text (16):

After the first array of NMR signals Z.sub.1 have been acquired and stored, a second array of signals Z.sub.2 are acquired. This is done during a scan in which the pulse sequence of FIG. 3A is employed, but the gradient moment G.sub.M is altered as shown in FIG. 3C to produce a moment of -.DELTA.M.sub.1. This is accomplished with gradient pulse 312 and 313 which are identical, but opposite in direction to the gradient pulses 310 and 311. After the 256 NMR signals Z.sub.2 have been acquired and stored in the computer 101, the data acquisition phase is completed for one axis of motion and the data processing phase is commenced.

Detailed Description Text (17):

It should be apparent to those skilled in the art that many variations in the data acquisition phase of the invention are possible. Other NMR pulse sequences can be employed, and as was mentioned previously, the acquisition of the k-space NMR data sets Z.sub.1 and Z.sub.2 can be interleaved. Also, multiple sequences may be conducted at each phase encoding gradient G.sub.y in order to improve signal-to-noise or to cancel system errors as described in U.S. Pat. No. 4,443,760. There are also many different ways to produce the gradient moment .DELTA.M.sub.1 using the gradient G.sub.M. For example, the gradient pulses 310-313 can be shaped differently, or they may be separated in time to increase the first moment .DELTA.M.sub.1. Also, it is possible to employ spin echo sequences which use 180.degree. RF pulses to refocus the undesirable effects of static magnetic field inhomogeneities. If 180.degree. pulses are used, as is known to those skilled in the art, the first moment can be produced by gradient lobes of the same polarity placed on opposite sides of the 180.degree. RF pulse.

Detailed Description Text (18):

In one preferred embodiment of the invention three pairs of k-space NMR data sets are acquired as described above. The first pair (Z.sub.1 (x) and Z.sub.2 (x)) have a gradient first moment G.sub.M directed along the x axis, the second pair (Z.sub.1 (y) Z.sub.2 (y)) have a gradient first moment G.sub.M directed along the y axis, and the third pair (Z.sub.1 (z) and Z.sub.2 (z)) have a gradient first moment G.sub.M directed along the z axis. As will be explained below, these pairs of k-space NMR data sets are processed separately according to the present invention and the results are then combined to form an angiogram which is sensitive to spins moving in any direction.

Detailed Description Text (19):

While a six point method for measuring the velocity of spins is described above, the present invention is also compatible with the simple four point method of three-dimensional flow measurement. In such case, the three data sets Z.sub.2 (x), Z.sub.2 (y) and Z.sub.2 (z) are replaced by a single data set Z.sub.2 (ref) which is produced using a flow compensated pulse sequence that is insensitive to motion along any axis. Both the six point and the balanced four point methods are described in our article in Society of Magnetic Resonance in Medicine, Ninth Annual Meeting, Abstract No. 475 (1990) entitled "Optimized Encoding For Phase Contrast Flow Measurement."

Detailed Description Text (20):

The processing of the k-space NMR data sets Z.sub.1 and Z.sub.2 to produce an angiogram is illustrated in FIG. 4. All of the processing is carried out in the main computer 101 under the direction of instructions in a stored program. The two k-space NMR data sets Z.sub.1 and Z.sub.2 are stored as 256 by 256 arrays of complex numbers indicated by blocks 320 and 321. The first step in the process is to perform a two-dimensional, complex Fourier transformation on each of these data sets 320 and 321 to transform the images they represent from k-space to the image domain. This is the same transformation used to produce conventional NMR images and the results are two 256 by 256 element arrays 322 and 323 of complex numbers (M.sub.1) and (M.sub.2). The magnitudes of the complex numbers M.sub.1 (x,y) and M.sub.2 (x,y) indicate the spin density at corresponding image pixel locations (x,y) and the phase of each complex number M.sub.1 (x,y) and M.sub.2 (x,y) is determined by both the velocity of the spins along the direction of the motion encoding magnetic field gradient G.sub.M and by any system phase errors. Any difference in these system phase errors in the two data sets produce image artifacts when a conventional complex-difference angiogram is produced using the image domain NMR data sets M.sub.1 and M.sub.2, and it is these phase errors which are substantially reduced by employing the teachings of the present invention.

Detailed Description Text (21):

Referring still to FIG. 4, phase corrections are calculated from the image domain NMR data sets 322 and 323. More specifically, a 256 by 256 element phase difference array 325 is calculated from the two transformed NMR data sets M.sub.1 and M.sub.2. Each element (.phi.) of the phase difference array 325 is calculated from the corresponding I.sub.1, Q.sub.1 and I.sub.2, Q.sub.2 elements of the respective data sets 322 and 323 as follows: ##EQU1## The .phi. values above are preferably computed using a four quadrant arctangent.

Detailed Description Text (23):

Where x and y are position in the two imaging coordinates. While the method



described herein is general enough to be compatible with nearly any phase correction method, in the preferred embodiment  $\phi_{sub.1}$ ,  $\alpha$  and  $\beta$  are calculated using a least squares fit. It has been found that weighting the least square fit by the square of the average magnitude  $A = (\frac{M_{sub.1}}{M_{sub.2}}) / 2$  provides adequate suppression of regions of low signal. Thus, the least squares fit for  $\phi_{sub.0}$ ,  $\alpha$  and  $\beta$  is:  $\sum_{x,y} (A^2 (\phi_{sub.0} - \alpha - \beta))^2$ . The summations in the above equations are over all pixel values in the image array. The corrected phase  $\phi_{sub.cor}$  is thus calculated for each position  $x, y$  in the array 326 using Eq. 1, where  $\phi_{sub.0}$ ,  $\alpha$ , and  $\beta$  were calculated using the average magnitude values ( $A$ ) and the phase difference values  $\phi_{sub}$  from the array 325. One important advantage of performing the phase correction on the phase image is that the correction can easily be extended to orders higher than linear.

#### Detailed Description Text (24):

A complex difference NMR data set is now calculated using the image domain NMR data sets 322 and 323, and the corrected phase difference array 326. This is accomplished by calculating each of 256 by 256 elements ( $D$ ) in a complex difference data set 330 using the corresponding elements  $M_{sub.1}$ ,  $M_{sub.2}$  and  $\phi_{sub.cor}$  in the respective arrays 322, 323 and 326 and the following formula:  $D = M_{sub.1} e^{i\phi_{sub.cor}} - M_{sub.2} e^{i\phi_{sub.0}}$ . In other words, the magnitude data in the image domain NMR data sets 322 and 323 is used, but the phase difference information is not used. Instead, the corrected phase difference data  $\phi_{sub.cor}$  in the array 326 is employed so that artifacts produced by phase errors are eliminated from the resulting angiogram.

#### Detailed Description Text (25):

If motion in all directions was encoded, the above procedure is repeated for each axis of motion ( $x, y$  and  $z$ ) to produce two more 256 by 256 element complex difference NMR data sets 331 and 332. The difference information in the arrays 330-332 thus indicate the complex differences  $D_{sub.x}$ ,  $D_{sub.y}$  and  $D_{sub.z}$  attributable to the motion of spins along the respective  $x, y$  and  $z$  axis. These are combined to produce a 256 by 256 element angiogram NMR data set 335 in accordance with the following formula:  $A = \sqrt{D_{sub.x}^2 + D_{sub.y}^2 + D_{sub.z}^2}$ . The angiogram NMR data set 335 may be used to produce a display in which moving spins are brighter than stationary spins. Since the motion of blood through the cardiovascular system is the predominant motion, the angiogram is essentially an image of the cardiovascular tree that is within the field of view.

#### Other Reference Publication (2):

C. B. Ahn & Z. H. Cho, "A New Phase Correction Method in NMR Imaging Based on Autocorrelation and Histogram Analysis", (Mar. 1987), pp. 32 & 36.

#### Other Reference Publication (3):

Bernstein, Thomasson & William, "Improved Detectability in Low Signal-to Noise Ratio Magnetic Resonance Images by Means of a Phase-Corrected Real Reconstruction", (Jul. 1989), pp. 813-817.

#### CLAIMS:

1. An NMR system for producing an angiogram with reduced sensitivity to unwanted phase shifts, the combination comprising:

means for applying a polarizing magnetic field to a region of interest;

means for applying a magnetic field gradient to the region of interest;

means for applying an RF excitation field to the region of interest;

means for acquiring an NMR signal produced by excited spins in the region of interest;

means for executing a first scan in which a first motion encoding magnetic field gradient is employed and in which the acquired NMR signals are stored as a first k-space NMR data set ( $Z_{sub.1}$ );

means for executing a second scan in which a second motion encoding magnetic field gradient is employed and in which the acquired NMR signals are stored as a second k-space NMR data set ( $Z_{sub.2}$ );

means for producing a corrected complex difference NMR data set from the k-space NMR

data sets (Z.sub.1) and (Z.sub.2)

which includes:

- a) means for producing a first image domain NMR data set (M.sub.1) by performing a Fourier transformation on the first k-space NMR data set (Z.sub.1);
  - b) means for producing a second image domain NMR data set (M.sub.2) by performing a Fourier transformation on the second k-space NMR data set (Z.sub.2);
  - c) means for calculation a phase difference array (.phi.) in which the value of each element therein is calculated from the values of corresponding elements in the first and second image domain NMR data sets (M.sub.1) and (M.sub.2);
  - d) means for calculating a corrected phase difference array (.phi..sub.cor) in which the value of each element therein is calculated from the value of the corresponding element in the phase difference array (.phi. );
  - e) means for calculating the complex difference NMR data set in which each element therein (D) is calculated from corresponding elements in the first and second image domain NMR data sets M.sub.1 and M.sub.2 and the corrected phase difference array (.phi..sub.cor) in accordance with the following expression: ##EQU5## means for producing an image in which the brightness of the pixels therein are determined by the values in the complex difference NMR data set.
2. The NMR system as recited in claim 1 in which the first and second motion encoding magnetic field gradients are applied separately along each of three axes of motion and the NMR system includes means for calculating a complex difference NMR data set (D.sub.x), (D.sub.y) and (D.sub.z) for each of said three axes of motion, and the means for producing the image combines the data from corresponding elements of the three complex difference NMR data sets (D.sub.x), (D.sub.y) and (D.sub.z) to determine the brightness of the image pixels.

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## Search Results - Record(s) 1 through 11 of 11 returned.

☐ 1. Document ID: US 20030022314 A1

L25: Entry 1 of 11

File: PGPB

Jan 30, 2003

PGPUB-DOCUMENT-NUMBER: 20030022314  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20030022314 A1

TITLE: Human chemokine beta-10 mutant polypeptides

PUBLICATION-DATE: January 30, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Olsen, Henrik S.	Gaithersburg	MD	US	
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Gentz, Solange H. L.	Rockville	MD	US	
Alderson, Ralph	Gaithersburg	MD	US	
Li, Yuling	Germantown	MD	US	
Parmelee, David	Rockville	MD	US	
White, John R.	Coatesville	PA	US	
Appelbaum, Edward R.	Blue Bell	PA	US	

US-CL-CURRENT: 435/69.5; 435/320.1, 435/325, 530/351, 536/23.5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
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☐ 2. Document ID: US 20020187950 A1

L25: Entry 2 of 11

File: PGPB

Dec 12, 2002

PGPUB-DOCUMENT-NUMBER: 20020187950  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20020187950 A1

TITLE: Keratinocyte derived interferon

PUBLICATION-DATE: December 12, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
LaFleur, David W.	Washington	DC	US	
Moore, Paul A.	Germantown	MD	US	
Ruben, Steven M.	Olney	MD	US	

US-CL-CURRENT: 514/44; 424/85.5, 435/320.1, 435/325, 435/69.51, 530/351, 536/23.5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWC
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☐ 3. Document ID: US 20020177551 A1

L25: Entry 3 of 11

File: PGPB

Nov 28, 2002

PGPUB-DOCUMENT-NUMBER: 20020177551

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020177551 A1

TITLE: Compositions and methods for treatment of neoplastic disease

PUBLICATION-DATE: November 28, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Terman, David S.	Pebble Beach	CA	US	

US-CL-CURRENT: 514/12; 435/325, 530/350

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWC
Draw Desc	Image										

☐ 4. Document ID: US 20020061834 A1

L25: Entry 4 of 11

File: PGPB

May 23, 2002

PGPUB-DOCUMENT-NUMBER: 20020061834

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020061834 A1

TITLE: Human G-protein Chemokine receptor (CCR5) HDGNR10

PUBLICATION-DATE: May 23, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rosen, Craig A.	Laytonsville	MD	US	
Roschke, Viktor	Rockville	MD	US	
Li, Yi	Sunnyvale	CA	US	
Ruben, Steven M.	Olney	MD	US	

US-CL-CURRENT: 514/1; 435/320.1, 435/325, 435/69.1, 530/350, 536/23.5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWC
Draw Desc	Image									

☐ 5. Document ID: US 20020048786 A1

L25: Entry 5 of 11

File: PGPB

Apr 25, 2002

PGPUB-DOCUMENT-NUMBER: 20020048786

PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20020048786 A1

TITLE: Human G-protein Chemokine Receptor HDGNR10

PUBLICATION-DATE: April 25, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rosen, Craig A.	Laytonsville	MD	US	
Roschke, Viktor	Rockville	MD	US	
Li, Yi	Sunnyvale	CA	US	
Ruben, Steven M.	Olney	MD	US	

US-CL-CURRENT: 435/69.1; 424/130.1, 435/325, 435/7.2, 514/12, 536/23.5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMOC
Draw Desc	Image									

☐ 6. Document ID: US 6472512 B1

L25: Entry 6 of 11

File: USPT

Oct 29, 2002

US-PAT-NO: 6472512

DOCUMENT-IDENTIFIER: US 6472512 B1

TITLE: Keratinocyte derived interferon

DATE-ISSUED: October 29, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
LaFleur; David W.	Washington	DC		
Moore; Paul A.	Germantown	MD		
Ruben; Steven M.	Olney	MD		

US-CL-CURRENT: 530/388.2; 435/331, 435/335, 435/7.92, 530/388.15, 530/389.2, 530/391.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMOC
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☐ 7. Document ID: US 6433145 B1

L25: Entry 7 of 11

File: USPT

Aug 13, 2002

US-PAT-NO: 6433145

DOCUMENT-IDENTIFIER: US 6433145 B1

TITLE: Keratinocyte derived interferon

DATE-ISSUED: August 13, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
LaFleur; David W.	Washington	DC		
Moore; Paul A.	Germantown	MD		
Ruben; Steven M.	Olney	MD		

US-CL-CURRENT: 530/351; 424/85.4, 435/7.1, 530/350

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KWMC

☐ 8. Document ID: US 6391589 B1

L25: Entry 8 of 11

File: USPT

May 21, 2002

US-PAT-NO: 6391589

DOCUMENT-IDENTIFIER: US 6391589 B1

TITLE: Human chemokine beta-10 mutant polypeptides

DATE-ISSUED: May 21, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Olsen; Henrik S.	Gaithersburg	MD		
Li; Haodong	Gaithersburg	MD		
Adams; Mark D.	North Potomac	MD		
Gentz; Solange H. L.	Rockville	MD		
Alderson; Ralph	Gaithersburg	MD		
Li; Yuling	Germantown	MD		
Parmelee; David	Rockville	MD		
White; John R.	Coatsville	PA		
Appelbaum; Edward R.	Blue Bell	PA		

US-CL-CURRENT: 435/69.5; 424/85.1, 435/252.3, 435/254.11, 435/320.1, 435/325, 435/471, 435/71.1, 435/71.2, 514/12, 514/2, 514/8, 530/324, 536/23.1, 536/23.5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KWMC

☒ 9. Document ID: US 6368275 B1

L25: Entry 9 of 11

File: USPT

Apr 9, 2002

US-PAT-NO: 6368275

DOCUMENT-IDENTIFIER: US 6368275 B1

TITLE: Method and apparatus for diagnostic medical information gathering, hyperthermia treatment, or directed gene therapy

DATE-ISSUED: April 9, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sliwa; John W.	Los Altos	CA		
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US-CL-CURRENT: 600/437; 600/302, 600/458, 600/549

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 10. Document ID: US 6231516 B1

L25: Entry 10 of 11

File: USPT

May 15, 2001

US-PAT-NO: 6231516

DOCUMENT-IDENTIFIER: US 6231516 B1

TITLE: Endoluminal implant with therapeutic and diagnostic capability

DATE-ISSUED: May 15, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Keilman; George W.	Woodinville	WA		
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US-CL-CURRENT: 600/485; 600/481

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 11. Document ID: US 5885829 A

L25: Entry 11 of 11

File: USPT

Mar 23, 1999

US-PAT-NO: 5885829

DOCUMENT-IDENTIFIER: US 5885829 A

TITLE: Engineering oral tissues

DATE-ISSUED: March 23, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mooney; David J.	Ann Arbor	MI		
Rutherford; Robert B.	Ann Arbor	MI		

US-CL-CURRENT: 435/325; 424/422, 424/435, 424/49, 435/374, 435/378, 435/69\_1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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MAGNITUDE.DWPI,TDBD,EPAB,JPAB,USPT,PGPB.	401086
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(24 AND MAGNITUDE).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	11
(L24 AND (MAGNITUDE)).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	11

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L25: Entry 9 of 11

File: USPT

Apr 9, 2002

DOCUMENT-IDENTIFIER: US 6368275 B1

TITLE: Method and apparatus for diagnostic medical information gathering, hyperthermia treatment, or directed gene therapy

Detailed Description Text (2):

Magnetic resonance imaging ("MRI") and ultrasound may be used to measure or map temperature in the human body. Ultrasound has also been used to map pressure in the body. With MRI, a thermally sensitive contrast agent has been demonstrated. Pressure information, such as ultrasound-derived blood pressures in the heart's chambers, may allow cardiologists to better assess the health and performance of the cardiovascular system. Temperature monitoring using either MRI or ultrasound on a fine scale may be extremely useful for the control of a variety of tissue-heating or cooling therapies designed to kill cancer, such as hyperthermia as done by ultrasound, microwave or RF heating of targeted tissue. A real-time (e.g. several samples per second) temperature mapping capability may aid in these and other developing treatments.

Detailed Description Text (5):

The micro-instruments 100 are fabricated from materials such as silicon, silicon dioxide, silica glasses, nitrides, thin-film metals or other materials, such as are currently used in semiconductor manufacturing and MEMS. The micro-instruments 100 made of such materials may or may not be biodegradable. For some materials the micro-instrument 100 is rendered biocompatible by coating with a biocompatible coating, such as titanium, polyethylene, parylene or other biological coatings known to be biocompatible.

Detailed Description Text (6):

Micro-instruments 100 particularly those without electronic circuitry or other electronic elements, may be fabricated using materials such as glasses that slowly dissolve. Such slow dissolving glasses are used in radioactive seed implants. Alternatively, salt crystals that are ultimately absorbed in the bloodstream are used.

Detailed Description Text (53):

Referring to FIG. 5, a section of a living body 510 is shown with a heart 512 and a plurality of micro-instruments 100 in the blood stream and the heart. A probe 500 is placed against the body 510. The ultrasonic imaging probe 500 includes a cable 506, a transmitter 502, and a receiver 504. The transmitter 502 emits an acoustic signal into the body. The receiver 504 receives a response signal from the micro-instruments 100. The transmitter 502 and receiver 504 are the same or different devices, such as an array of piezo-electric elements. The piezo-element(s) may also form the ultrasound imaging array or may be independent from the array. Alternatively, the micro-instrument 100 can generate the response signal without receiving an acoustic signal. That is, the micro-instrument 100 automatically transmits. In alternative embodiments, the transmitter and receivers are electromagnetic in nature for MRI, CAT scan, PET, optical, x-ray or other imaging.

Detailed Description Text (56):

The output of the receive beamformer 516 is electrically connected with a scan converter 518. The scan converter comprises devices for detecting and formatting the data for display as an image. Any of various ultrasound systems may be used, such as

the Acuson ultrasound systems with the tradenames 128XP, Aspen or Sequoia, or ultrasound systems made by other manufacturers. In alternative embodiments, the probe 500, transmitter 502, receiver 504, transmit and receive beamformers 514 and 516 and/or scan converter 518 comprise devices for CRT, MRI or CAT scan imaging. The receiver 504 and transmitter 502 are conveniently located in transducer 500, but may be located elsewhere in the system.

Detailed Description Text (57):

For imaging, a single micro-instrument 100 or hundreds or more of the micro-instruments 100 are administered or placed within the body 510. The micro-instruments 100 may conveniently be injected, as are conventional contrast agents, into the bloodstream. For example, the micro-instruments 100 are suspended in conventional solutions of saline and wetting agents as desired. In alternative embodiments, the micro-instruments 100 are administered in any other acceptable manner including propelling into tissue, swallowing, inhalation, urethrally, annally or using a needle. For example, when prostate cancer is treated by hyperthermia microwave treatment, the micro-instruments 100 are injected directly into the prostate gland and the surrounding tissues, preferably using a hollow needle.

Detailed Description Text (58):

The density of micro-instruments 100 is less than, the same as, or greater than the density of conventional contrast agents. The density of micro-instruments 100 in a portion of the body is preferably between 1 and 1.times.10.sup.+9 micro-instruments per cubic centimeter. To measure pressure with a resolution of 1 mm in 3 dimensions, micro-instrument density can be on the order of only 1,000 micro-instruments per cubic centimeter, several orders of magnitude lower than for conventional agents.

Detailed Description Text (71):

Second, an optional initiation signal is transmitted into the body at 704. The initiation signal is generated external to the body 510 or by another micro-instrument 100 catheter or other device in the body 510. Then, at least one response signal from at least one of the plurality of micro-instruments is received at 706. The response signal is preferably received external to the body 510, but may be received by a device within the body 510. The response signal varies as a function of a characteristic of a portion of the body near the micro-instrument 100 in this case pressure. If an initiation signal is not transmitted, then the signal generated in step 706 may be automatically generated.

Other Reference Publication (12):

Jacco A. De Zwart; Fast Magnetic-Resonance Temperature Imaging; Apr. 29, 1996; pp. 86-90.

Other Reference Publication (14):

Kagayaki Kuroda; Temperature Mapping Using the Water Proton Chemical Shift: A Chemical Shift Selective Phase Mapping Method; 1997; pp. 845-851.

CLAIMS:

2. The device of claim 1 wherein the observable property comprises a property observable in a modality selected from the group consisting of: ultrasound, magnetic resonance, computerized axial tomography, PET, x-rays and optical imaging.